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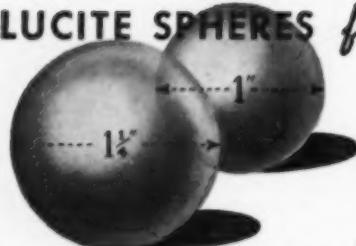


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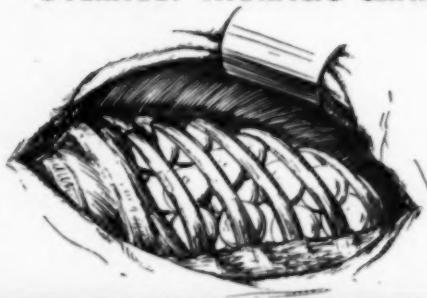
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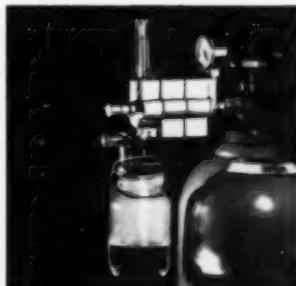
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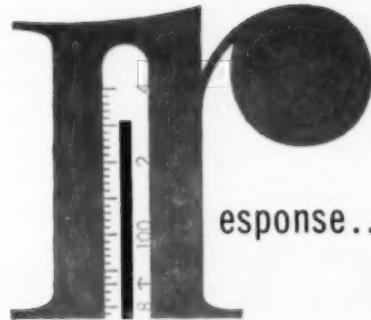
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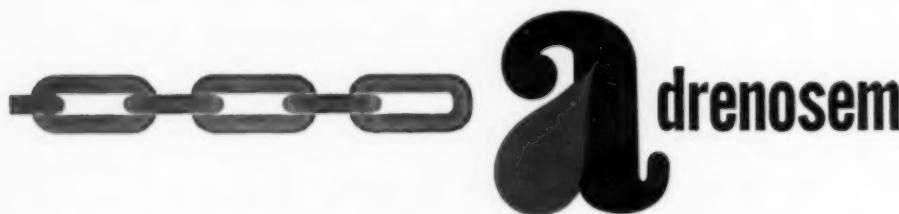
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1. Hobby, G. L., Lenert, T. F., Rivoire, Z. C., Donikian, M., and Pikula, D.: Am. Rev. Tuberc. 67:808, 1953.

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*Heck, W.E.; Lynch, W.J., and Graves, H.L.: *Acta oto-laryng.* 40:416, 1953.

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1. Rudin, L. N., and Jensen, J. R., C. M. Digest, XX: 7, 1953
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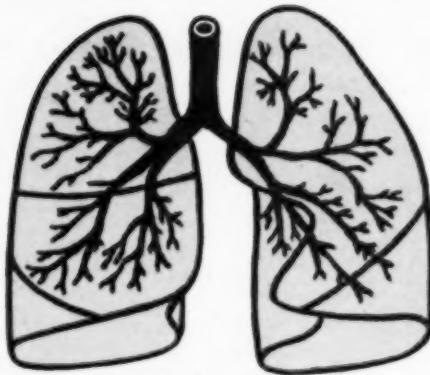
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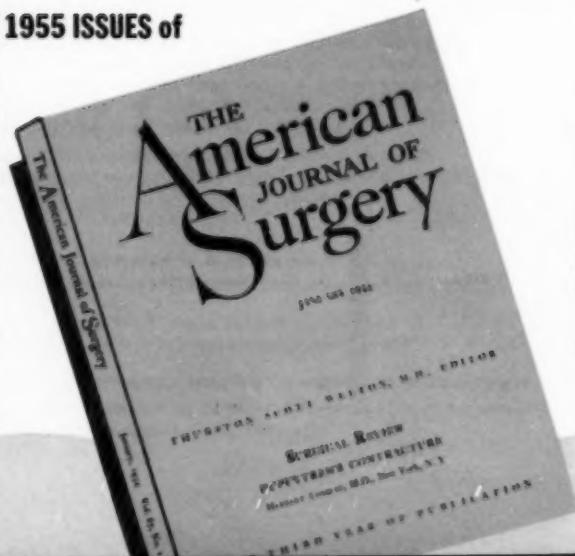
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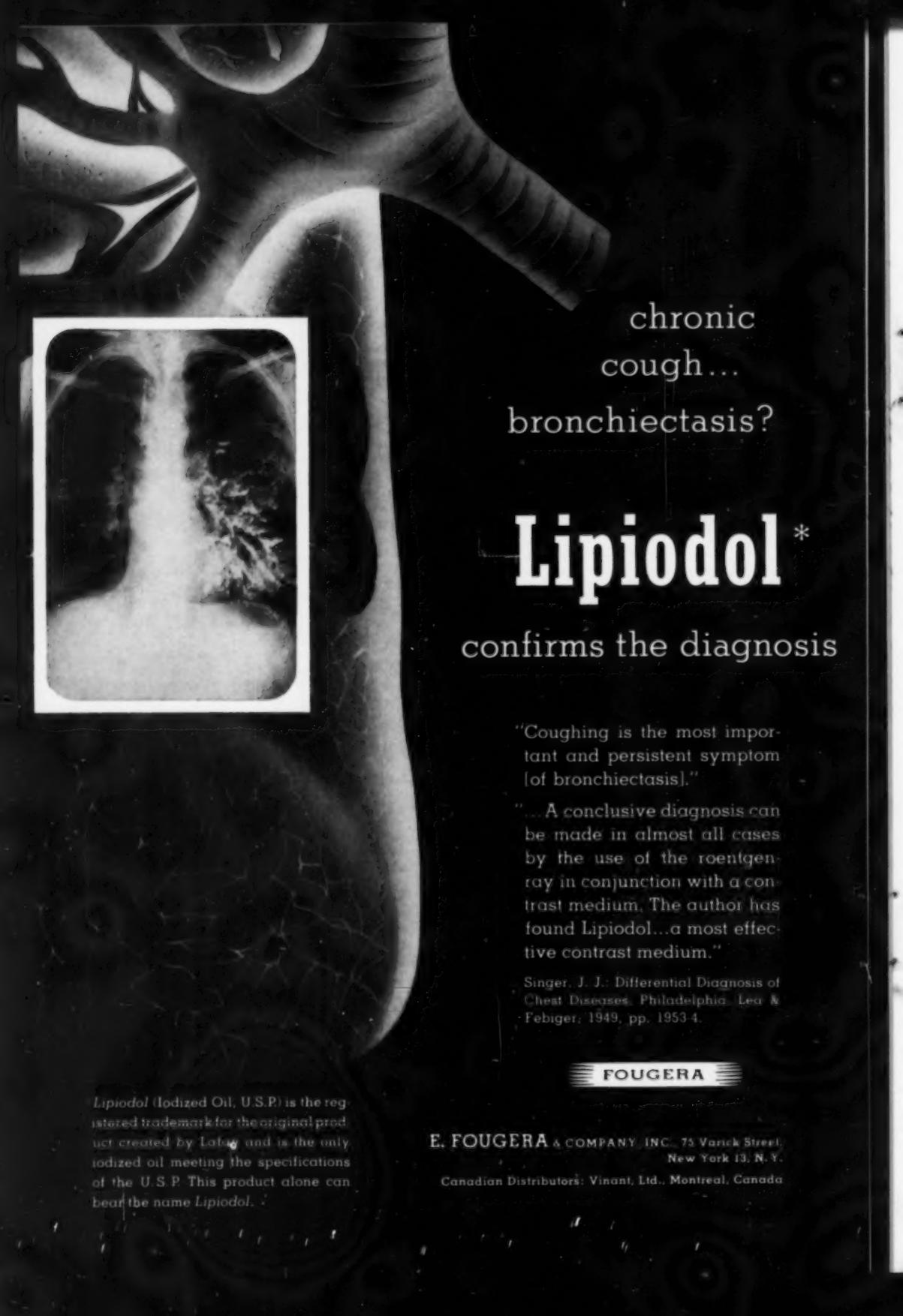
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1. Scheifley, C. H.: GP 2:59 (July) 1950

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References

(1) Kirby, W. M. M.; Waddington, W. S., & Doornink, G. M.: Antibiotics Annual, 1953-1954, New York, Medical Encyclopedia, Inc., 1953, p. 285. (2) Finland, M., & Haight, T. H.: *Arch. Int. Med.* 91: 143, 1953.

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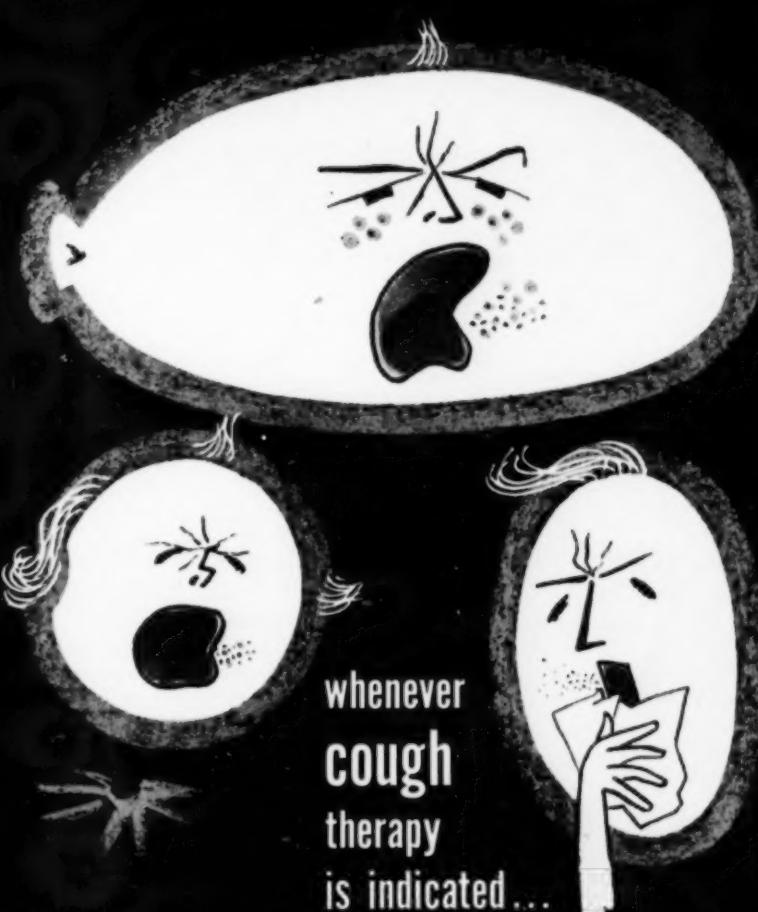
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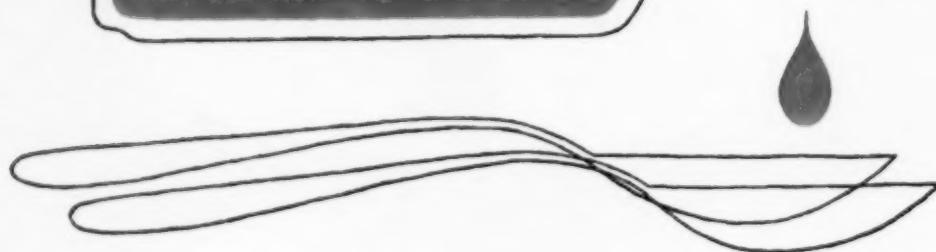
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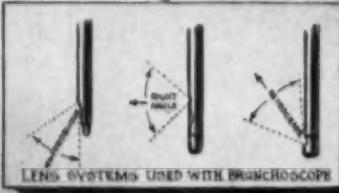
XRAY INDICATES PATHOLOGY IN UPPER LOBE
BUT NOT DIAGNOSTIC OF NEOPLASM

Bronchus to upper left lobe



VIEW OBTAINED WITH RIGHT ANGLE TELESCOPE

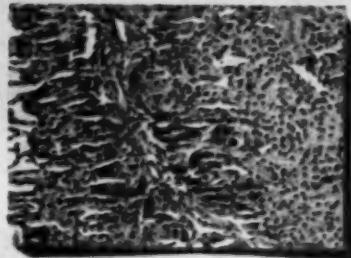
Right bronchus



Bronchus
to lower
lobe

Obtaining view of tumor in bronchus to
upper lobe of left lung with right angle
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1. Flippin, H. F.: Postgrad. Med. 14:6 (July) 1953
2. Flippin, H. F., et al.: J.A.M.A. 147:918 (Nov. 3) 1951
3. Finberg, L., et al.: Antibiot. & Chem. 3:353 (April) 1953





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DISEASES of the CHEST

VOLUME XXVI

NOVEMBER 1954

NUMBER 5

Cardiac Standstill*

K. V. S. RAO, M.D., W. L. JAMISON, M.D., F.C.C.P.,
H. E. BOLTON, M.D., F.C.C.P. and J. E. RUBEN, M.D.

Philadelphia, Pennsylvania

Few episodes in the lifetime of a surgeon could be more dramatic than that of seeing a heart which has completely stopped beating return to normal rhythm and force, followed by complete recovery of the patient. Two unusual episodes occurred recently in the authors' practice and form the basis of this report. Both of these patients recovered without brain damage.

The first death due to cardiac arrest under anesthesia was reported in 1848.¹ History has it that cardiac massage was used for cardiac standstill for the first time, but unsuccessfully, in 1889 by Nichaus. It was carried out successfully by Inelsand in 1901, followed by Starling and Lane in 1902, and subsequently by others.

Since increasing occurrences of cardiac standstill are being reported, the number of cases in the literature is now over 300. This indicates that it occurs not infrequently and may happen during or following anesthesia for any procedure. Occasionally, cardiac standstill occurs in the absence of heart disease as a terminal event in peripheral vascular collapse, trauma, accidental suffocation, drowning, or electric shock. In patients with complete heart block it may be transient, causing the Stokes-Adams syndrome.

Problem of Cardiac Arrest

To date cardiac standstill is a serious, usually terminal, event that rarely responds to currently employed therapeutic measures. Hence, it is a problem of the first magnitude, taxing the ingenuity of the surgeon, anesthetist, resident, and nurse.

The condition poses two problems²:

(1) The heart must be restarted.

(2) The central nervous system must not be deprived of oxygenated blood for more than three or four minutes. Cerebral anemia of longer duration is followed by widespread destruction of the cerebral cortex, manifested clinically by signs of decerebrate rigidity often without microscopic or macroscopic changes in the brain at autopsy.³

In those cases in which resuscitation is possible after cardiac arrest,

*From the Charles P. Bailey Thoracic Clinic and Doctors' Hospital and with the Support of the Mary Bailey Foundation for Heart and Great Vessel Research, Philadelphia, Pa.

failure is due to delay in diagnosis and in institution of proper treatment.

Other causes, as outlined by Fauteux,⁴ are hyperirritability of the heart and peripheral circulatory failure.

Peripheral circulatory failure may develop after long trials at resuscitation. It may be that co-ordinated beats are restored and seem to have sufficient strength to propel the blood, yet the pressure remains at zero or at a very low level. Infusion of 500 cubic centimeters of whole blood directly into the exposed aorta while massaging the heart may result in satisfactory elevation of the pressure which will remain when the heart is left to work by itself.

Signs of Standstill

Premonitory signs are slowing and weakening of the pulse and heart beat, hypotension, and cyanosis. The cessation of heart beat may be caused by either cardiac arrest, or ventricular fibrillation. The general management of cardiac standstill as carried out by the authors is as follows:

Management of Cardiac Standstill

A well organized plan of handling cardiac standstill should be developed.^{3, 5} No time should be lost in useless discussion by members of the operating team. All, or as many as possible, in the departments of surgery and anesthesiology should be trained in the proper method of cardiac resuscitation. In an emergency, it is a question of "getting all hands to the pump."

Nothing will be accomplished by rechecking blood pressure that has been non-existent for two or three minutes. The only certain method of ascertaining whether the heart is still beating is to palpate or visualize it or the large arteries directly.² Cardiac action may be assumed to have ceased if carotid artery pulsations are not palpable.⁵ If the heart has stopped beating or the ventricles are fibrillating, minutes can be saved by rapidly opening the chest for diagnosis; if the heart is still beating feebly, little harm will have been done by the procedure.² The authors have found the transthoracic approach the quickest and most effective route to the heart. The important thing is to get the hand quickly to the heart and start massaging while the anesthetist inserts an endotracheal tube and inflates the lungs with 100 per cent oxygen. After thoracotomy is quickly performed, the pericardium is opened and it is determined by inspection and palpation whether the heart is in cardiac arrest or ventricular fibrillation.

Cardiac Arrest

If, upon opening the chest the heart is in arrest as shown by complete absence of contractions, or is in dire trouble as shown by regular but feeble and ineffective contractions, treatment is carried out in the following manner. The keynotes are time, massage, and oxygen.

Cardiac massage is started immediately. This may be performed with

either hand or with both. The objective is to institute contraction effective enough to maintain the blood flow to the brain. The rate of cardiac massage must be adjusted to that which allows filling of the ventricles before compression of them. The most rapid rate which allows for filling should be used.

An intratracheal tube is inserted as quickly as possible, by a trained anesthetist if available. The lungs are inflated with oxygen through an anesthesia machine or an automatic respirator, such as Pneophore.* In the event trained help is not available, mouth-to-mouth breathing may be carried out.

Atropine sulfate 1/100 gr. (0.6 mgm.) is given intravenously.

If the tone of the heart muscle is flabby, epinephrine (1:1000) one cubic centimeter in 10 cubic centimeters of saline solution is injected into either the right or left ventricle (in spite of the dire warnings of the pharmacologists).

If citrated blood has been used in quantity, calcium chloride may be given, 3 cubic centimeters of a 10 per cent solution, every five minutes for a total dose of 10 cubic centimeters. This also will help restore tone and force of contraction.

Rapid restoration of the circulating blood volume should not be ne-



Five Technical Methods of Maintaining Respirations Are Shown in Figures 1 through 5.
FIGURE 1: Mouth-to-mouth breathing. The physician may compress the patient's nose, and exhale through gauze into the patient's mouth.

*Made by the Mine Safety Appliance Company, Pittsburgh, Pa.

glected. Not only has the actual volume been depleted, perhaps, by preceding blood loss or shock, but it is reduced functionally and immediately when the central circulatory mechanism, the heart, fails. Too often additions to the circulating blood volume may not proportionately raise the blood pressure because the vasomotor system rapidly becomes depressed during cardiac standstill. In such instances, the authors have found the rapid transfusion under pressure of 500 cubic centimeters of whole blood directly into the aorta or radial artery to be the most effective means of maintaining the heart beat and the blood pressure. Increasing the blood pressure in the aorta will, of course, increase the vital coronary and cerebral circulation.

Ventricular Fibrillation

Ventricular fibrillation is diagnosed as quivering of the heart muscle on inspection of the heart, and the sensation of a bag of worms on palpation. Ventricular fibrillation can be differentiated from arrest immedi-



FIGURE 2: If an intratracheal tube is available, mouth-to-mouth breathing may be carried out more efficiently through an intratracheal tube.

ately. An electrocardiogram is not necessary. Coarse fibrillation seems to be an earlier state than fine fibrillation and seems to have a better prognosis. The following treatment is instituted.

Steps 1 and 2 as given under cardiac arrest are carried out.

Cardiac massage as previously described is started. The authors do not feel that a heart can be defibrillated unless there is adequate pressure in the coronary arteries. Rapid, forceful, manual compression is necessary to elevate the coronary artery pressure. Clamping the descending aorta for up to 15 minutes will hasten this process.

Electric shock, using ordinary 110 volt, 60 cycle, alternating current, is then applied. The voltage required for enlarged pathologic hearts may be somewhat higher than this. Nurses assisting the authors are trained to keep the plug and receptacle in either hand, holding them apart until the command of "Hit" is given. The plug is then pushed into the receptacle and immediately withdrawn. This method has been used many times and the authors have had no trouble with shock even when bare-handed assistants touch the patient. Assistants whose hands are simultaneously in contact with metal and the patient may be shocked, but no shocks have been received by merely touching the patient.

Procaine, 5 cubic centimeters of 1 per cent solution, may be injected into the right or left ventricle.



FIGURE 3: An ordinary airway may be placed, and the mask of the Pneophore held in position, either manually or by strapping.

The authors do not hesitate to give epinephrine (one cubic centimeter of a 1-1000 solution, diluted with nine cubic centimeters of saline solution) into any heart that does not respond.

Calcium chloride in doses of 2 to 10 cubic centimeters of a 10 per cent solution, is injected into the left ventricle. The preferred amount is 3 cubic centimeters because large doses may cause tetanic contraction of the left ventricle.

Case Reports

Case 1: Case No. 26315 is rare in that it is the first successful cardiac massage after cardiac surgery performed while the patient was in bed in her room. This 19 year old housewife was operated on March 16, 1953 for mitral insufficiency. At operation, regurgitation estimated at 40 cubic centimeters per heart beat was encountered. The mitral valve was sutured and the operation was terminated without incident. The sutures were removed on April 1, and the postoperative course was uneventful. Fluoroscopy showed no pathology and the patient was considered ready to return home within the next few days. However, on April 2, at 6:50 P.M., her roommate observed that she suddenly became cyanotic and fell. The roommate ran to the nursing supervisor's desk. The thoracic surgical group happened to be making rounds and its members immediately rushed to the patient's room. The patient was cyanotic and was hanging from the edge of the bed with her head down. She was placed in a supine position and was found to be pulseless with widely dilated pupils and no heart beat. Her chest wound was promptly opened with a pair of bandage scissors.

The heart was in complete arrest, and cardiac massage was immediately started



FIGURE 4: An intratracheal tube may be placed and secured in position by a safety pin. The mask of the Pneophore is then applied over this.

and oxygen at a positive pressure of 20 to 30 centimeters of water was administered by a Pneophore.

Atropine, 0.4 mgm., was given intravenously. Following manual cardiac massage for three minutes and the injection into the left ventricle of 10 cubic centimeters of a 10 per cent solution of calcium chloride, the heart began to beat. Ventilation with 100 per cent oxygen was continued. The ribs were approximated with one pericostal suture and the chest wall was closed in layers. The skin was approximated with stainless steel wire. The patient's color improved; the pupils, which had been dilated, became normal in size again and reacted to light. She was still given oxygen under positive pressure and a close watch was kept on her respirations, blood pressure, and apical rate.

A second cardiac arrest occurred at 10 P.M. She became dyspneic and ceased breathing, and the heart suddenly stopped beating. The thoracic wound was opened by the resident (K. V. R.) and the heart was found to be in asystole. Massage was started and 0.4 mgm. of Atropine was given intravenously simultaneously. The lungs were ventilated with oxygen under positive pressure (equivalent to 20 to 30 centimeters of water) by an anesthetist. The heart began to beat and its contractions became fairly vigorous. The chest was closed, using chromic catgut No. 2 for the pericostal suturing, a running stitch of No. 1 chromic catgut in the muscles, and wire in the skin. Administration of oxygen under positive pressure (10 to 15 centimeters of water) by means of a Pneophore, was continued, and 0.4 mgm. of Atropine with 30 mgm. of Papaverine was administered intramuscularly every four hours.

Chest instruments for immediate thoracotomy and possible arterial embolectomy were kept in the patient's room. Special nurses cared for the patient for the next 48 hours. Within two hours (at 12 o'clock midnight), the patient was able to open her eyes, but could not talk.

The next morning, she responded better and on questioning said she felt fine. Roentgenograms taken that morning (April 3) revealed a fair degree of pneumothorax over the left upper lobe, and a density at the left base suggestive of fluid.

The total white blood cell count taken during the period of cardiac standstill on April 2 showed 28,200 leukocytes per cubic millimeter; the hemoglobin was 68 per cent.

It was felt that, in view of the high white cell count and low hemoglobin, pulmonary

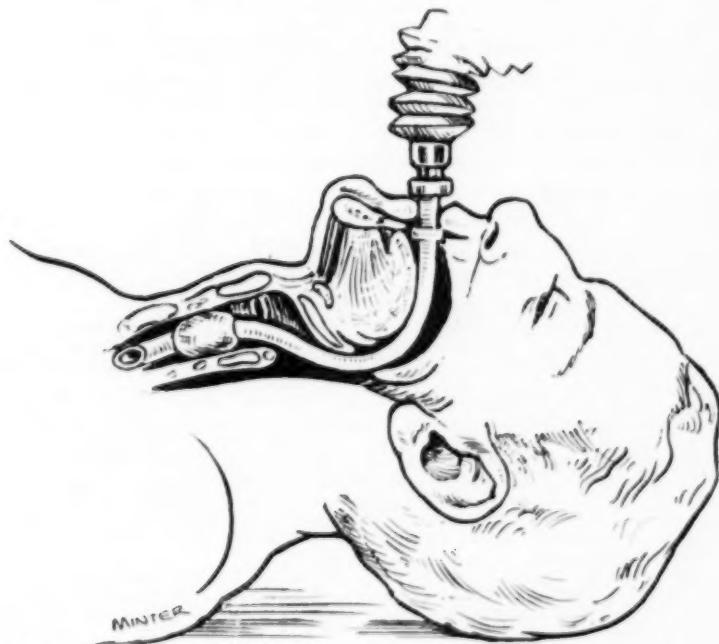


FIGURE 5: An intratracheal tube having an inflatable rubber cuff may be placed and this can be attached to the Pneophore directly.

embolism should be considered as a possible cause of the cardiac standstill.

This was confirmed 48 hours later when she coughed up blood in sputum and the white cell count rose to 32,400. The hemoglobin at that time was 77, and so no blood transfusion was given.

On April 3, by 9 P.M., her respirations had increased to 64 per minute, and her temperature was 102° F. It was felt that retained secretions in the bronchial tree might be responsible for the increased respiratory rate. Atropine 0.4 mgm. was given intravenously, followed by bronchoscopy. Both the left main bronchus and the bronchi of the left lower lobe were filled with bloody secretions and blood clots were found in the left lower lobe. All bronchi were aspirated free of secretions. Oxygen was given through the bronchoscope during the entire procedure. Epinephrine, 1:1000 was applied with cotton sponges to the lower lobe bronchus. Her breathing was considerably relieved, and the color of her face and fingernails became pink at the end of the procedure. There was little effect on the heart rate, and she was returned to her room improved. The temperature dropped to normal at the end of 24 hours.

Henceforth, her postoperative course was uneventful. It was surprising that she did not have any wound infection despite the chest's having been opened twice in bed with bandage scissors and massage having been carried out with the bare hands!

She was given Papaverine 30 mgm. with 0.4 mgm. Atropine every four hours intramuscularly from the night of April 2 until April 6. She was also maintained on a heavy regimen of antibiotics:

1. Penicillin Sodium 500,000 units every three hours.
2. Streptomycin 0.5 grams twice daily until April 7.
3. Terramycin 250 mgm. every four hours until April 6.

In order to lessen the threat of further pulmonary embolism, one dose of heparin (200 mgm.) was given, and 100 mgm. of dicumarol per day was started. Daily prothrombin times were done. She was also given digitoxin 0.2 mgm. daily from April 4. Her last dose of dicumarol was on April 9. Stitches were removed on April 14 and she was discharged from the hospital on the same day. Three weeks after discharge from the hospital, while she was at home, a similar episode occurred with fatal termination. No pathological or anatomical reason for this fatal outcome could be found at autopsy.

Comment

This case illustrates how cardiac standstill can occur twice during the postoperative course and how it can be treated successfully at the bedside, with complete restoration of cardiac function and without any damage on either occasion to the brain. It was surprising that despite two bouts of cardiac standstill during which the chest was opened with bandage scissors and massage was carried out with bare hands, no wound infection occurred. This also illustrates that complications (for example; retained secretions requiring bronchoscopy) should be treated as after any thoracotomy.

Case 2: Case no. 26450 is unusual in that the patient recovered after 50 minutes of cardiac arrest and ventricular fibrillation. R. G. was a 27 year old housewife who was operated by one of us (H. E. B.). Following successful dilatation of the mitral and aortic valves, it was felt that the tricuspid valve should be explored, since a suspicion of tricuspid stenosis was entertained from cardiac catheterization studies.

The exposure of the right auricular appendage through the left lateral thoracotomy incision (Fifth interspace) is not too satisfactory. Since the blood pressure was falling, the attempt at exploration of the tricuspid valve was abandoned, and the purse-string suture at the base of the right auricular appendage was tied securely. Everything went well up to this point. While the auricular appendage was being oversewn with No. 00 cotton, the heart went into sudden standstill (at 4:10 P.M.).

Cardiac massage was immediately instituted, and 0.4 mgm. of Atropine was given intravenously. The heart's action was resumed for a few beats and then gross ventricular fibrillation began.

Electrical defibrillation was applied, but due to inadvertent touching together of the two electrodes the electrical fuse burned out. Manual massage was carried on assiduously while the anesthesiologist ventilated the lungs with 100 per cent oxygen and pumped blood directly into the aorta. Intracardiac injection of 1 cubic centimeter of 1:1000 epinephrine was given. The heart showed gross fibrillations but as the fuse had blown and no alternating current was available, the defibrillators could not be used. As a desperate measure, 10 cubic centimeters of 10 per cent calcium

chloride was injected into the left ventricle and massage was continued. At 5 P.M., the heart reverted to sinus rhythm and was able to maintain its contractions. The heart was replaced in the pericardial sac and a further injection of 5 cubic centimeters of 10 per cent calcium chloride was given into the left ventricle. The heart now maintained its rhythm well and the first spontaneous respiration occurred at 5:10 P.M. The amount of time elapsing from the first cardiac standstill until the restoration of an independent heart beat was 50 minutes.

The polyethylene tube in the aorta which was used for transfusion, was removed and the opening closed with No. 000 Deknatol.

The pericardium was left open. The chest was closed rapidly, the skin being approximated with No. 28 stainless steel wire.

As soon as she was turned on her back at 5:15 P.M., she responded and asked, "Did I give you any trouble?"

At 5:20 P.M., she moved her extremities. Some time was spent in the operating room ventilating her lungs with oxygen. Her bed was taken to the operating room and she was transferred to it and returned to her room at 5:35 P.M. Strict orders were given not to turn her to the left side for fear of herniation of the heart through the open pericardium. From this point on, her postoperative course was no different from that of any other patient undergoing cardiac surgery. When returned to her room, her blood pressure was 90/60 mm. Hg.

At 6:45 P.M., her blood pressure fell to 80/60 mm. mercury; pulse was 40 per minute; apical rate was 148 and respirations were 48 per minute. At this point, she started to talk and complained of difficulty in breathing. An infusion of 500 cubic centimeters of 5 per cent dextrose in water, to which 20 mgm. of vasoxyl and 5 cubic centimeters of aqueous adrenal cortical extract were added, was run at 30 drops per minute until her blood pressure rose to 100 mm. systolic; at that point, the infusion was slowed to 20 drops per minute. By 7:45 P.M., she was able to take sips of water.

She had a fair night; however, by the following afternoon her respiration became labored at 48 per minute. Atropine 0.4 mgm. was given intravenously, followed by bronchoscopy. Large amounts of thick mucous were aspirated from the bronchi of the left lower lobe. After bronchoscopy, the rapid breathing quickly ceased. Dyspnea and cyanosis were relieved at the end of the procedure and she was returned to her room in good condition.

On the morning of March 21, she again had retention of secretions which were aspirated. Breathing improved. Oxygen under positive pressure was administered from time to time. The drainage tube was removed from her chest at the end of 48 hours.

Electrocardiograms taken four hours postoperatively were consistent with a normal sinus rhythm and some degree of myocardial depression. The latter were shown by the reduced amplitude of the QRS complexes, and the preponderant right ventricular pattern in the precordial leads. Those taken on March 24 were consistent with normal sinus rhythm. The findings were essentially normal except for some T-wave abnormalities in the limb leads.

Biopsy of the auricular appendage revealed active rheumatic endocarditis which might have been responsible for the elevated temperatures during the first week postoperatively. Sutures were removed on 16th postoperative day.

Right-sided pleural effusion which required thoracentesis on several occasions in no way interfered with subsequent recovery. She was discharged from the hospital on April 9, 1953.

Comment

A case of ventricular fibrillation responding after 50 minutes to the injection of calcium chloride is reported. The possibility that the administration of citrated blood directly into the aorta depressed the heart can not be overlooked as an etiologic factor.⁵ We believe that electric shock remains the treatment of choice in ventricular fibrillation in every situation where it can be performed. In the case above, it was not available.

SUMMARY

The history of physicians' attempts to deal with sudden death under anesthesia has been briefly sketched. We have described the method of managing cardiac arrest as practiced in the Charles P. Bailey Thoracic Clinic, and have differentiated this from the management of ventricular

fibrillation. We have also described the management of ventricular fibrillation.

Two unusual cases have been reported. In the first, cardiac arrest was overcome after cardiac surgery with the patient in bed in her room twice in less than four hours, with subsequent complete recovery without brain damage. The second patient had no spontaneous heartbeat for 50 minutes in the course of cardiac surgery, yet recovered completely with no brain or other tissue damage.

We have no desire to encourage indiscriminate attempts at cardiac resuscitation; but it is hoped that these two examples of the rewards of persistence once it has been undertaken in suitable candidates will encourage others. This may result in additional salvage of useful lives.

RESUMEN

Se esboza brevemente la historia de los esfuerzos de los médicos para hacer frente a la muerte súbita durante la anestesia. Hemos descrito el método para tratar el paro cardíaco en la Clínica de Tórax del Dr. Charles P. Bailey y lo hemos diferenciado del tratamiento de la fibrilación ventricular. También describimos el tratamiento de la fibrilación ventricular.

Los casos poco comunes hemos referido. En el primero, el paro fué dominado después de cirugía cardíaca, en su lecho en su habitación dos veces en menos de cuatro horas con recuperación sin daño cerebral.

El segundo no tuvo latidos espontáneos por 50 minutos en el curso de una operación de corazón, pero se recuperó completamente sin daño en el cerebro ni en otros tejidos.

No deseamos alentar los intentos indiscriminados para la resucitación cardíaca; pero se espera que estos dos ejemplos de resultados después la persistencia de los esfuerzos una vez emprendidos en sujetos adecuados, animen a otros. Esto puede dar más rescate de vidas útiles.

RESUME

Les auteurs rappellent rapidement les différentes conceptions successives sur la conduite à tenir lors d'une mort subite au cours de l'anesthésie. Ils exposent ce qui doit être fait en présence d'une syncope cardiaque, selon la pratique habituelle de la Clinique de Chirurgie Thoracique de Charles P. Bailey. Ils l'opposent à la conduite à tenir en cas de fibrillation ventriculaire. Ils décrivent par ailleurs l'attitude qu'il convient de prendre dans ce dernier cas.

Ils rapportent deux observations peu communes. Dans le premier cas, la syncope cardiaque survint après une intervention chirurgicale sur le cœur. La malade était dans son lit, revenue dans sa chambre, et l'accident se produisit deux fois en moins de quatre heures. Néanmoins, la malade se remit complètement, sans aucun trouble cérébral. Le second malade n'eut aucun battement cardiaque spontané pendant 50 minutes, au cours d'une intervention sur le cœur, et cependant, il guérit complètement sans aucune séquelle cérébrale ou d'autun autre organe.

Les auteurs se défendent de vouloir encourager des tentatives de rani-

mation cardiaque sans discrimination. Mais ils espèrent que ces deux exemples de persévérance dans la tentative en encourageront d'autres. Il pourra en résulter le sauvetage de vies utiles.

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The Cream-Egg Medium for Recovery and Enrichment of the Growth of Tubercl Bacilli from Septic Material *

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The need for a better medium to recover weakened or "latent" tubercle bacilli has become more desirable since there are so many reports of finding acid fast forms in sputum and resected specimens^{1, 2, 3, 4, 5} with little or no corresponding growth on cultures and, in some studies, little or no ill effects on susceptible animals. Most of these authors found only about 20 per cent of their smear-positive specimens, positive on culture or in animals. They recognize that many of the bacilli may have been dying for varying periods of time before the drug treatment and that it is difficult to assign the exact role of the chemical or antibiotic in the process. In fact Katz⁶ made a study of six resected lesions without drug treatment and obtained only a little higher percentage in positive findings than in the various reports on drug treated specimens. Of five cases with positive smear only two (40 per cent) grew on culture. The death of tubercle bacilli is only to be expected as any tuberculous patient recovers.

The question of the viability of these acid fast forms has been established for certain protoplasmic parts of the "latent" bacilli⁷ but there has not been complete success in causing these "sleepers" to reproduce. Although they may be dying and essentially dead, there is no justification in drawing that conclusion until every avenue has been explored.

Several years ago Stadnichenko, Sweany, and Kloeck⁸ in a study of tubercle bacilli in birds and mammals made an exhaustive search with many ingredients, and modified a cream-egg mixture proposed by Sweany and Evanoff⁹ that gave results which were superior to all other mediums of that time including the Lowenstein-Jensen¹⁰ combination as modified by Holmes.¹¹ There were several faults with the medium, however, and as a result it was not generally used. One of the principle difficulties was the uncertainty of obtaining a homogenous mixture. This drawback has now been corrected by use of the "Waring Blendor." The selection of fresh material as well as proper manipulation is obligatory and can be expected of all good bacteriological technicians. The recently proposed blood agar medium of Tarshis¹² is cheap and simple to prepare, but it has no more to offer than the Lowenstein medium so far as diagnostic possibilities are concerned.

Preparation of the Medium

The details of preparation of the medium are as follows:

Strictly fresh unpasteurized cream and milk, as well as fresh eggs are essential. Careful observance of sterile methods should be practiced.

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Work should be done in a closed, dust-free room; sterile gloves should be worn while handling the eggs after they are washed; and the open beakers and flasks should be exposed to the air for as short a time as possible, especially while breaking the eggs.

Some of the decimals in the formula may not be necessary but are included to bring the total amount to an even 100 per cent.

1. Formula of the medium:

(a) Percentage of ingredients by volume:

	Per Cent
egg yolk	42.5
egg white	19.2
milk	27.8
cream	9.3
2 per cent malachite green oxalate	1.2

(b) Percentage of dry ingredients by weight:

Potato flour	1.85 gms.
asparagin	0.18 gms.

2. Equipment required for preparation of 2 liters of medium:

Sterile rubber gloves and all sterile glassware including:

- 1 3 liter flask containing approximately 100 grams glass bead.
- 1 2 liter flask (no glass beads).
- 1 2 liter flask containing glass beads.
- 1 500 cc flask (no glass beads).
- 1 2 liter beaker marked at 850 cc level.
- 1 600 cc beaker marked at 384 cc level.
- 1 heavy glass rod (for mixing eggs in 2L beaker).
- 1 100 cc graduate, marked at 82 cc and 104 cc level.
- 1 dispensing burette, 1000 cc capacity. (See Cenco catalogue #16018).
- 1 Waring Blender.
- 1 knife for breaking eggs.
- 2 pots, sufficiently large to contain 52 eggs before breaking.
- 175 1 ounce, flat, screw cap bottles.

3. Preparation:

(a) *Cream:* Measure 104 cc. of cream (approx. 38 per cent butter fat) in sterile graduate and pour into sterile 500 cc. flask. Measure 82 cc. of milk (approx. 3.8 per cent butter fat) and pour into same 500 cc. flask.

This mixture results in approximately 23 per cent butter fat content. Mix well.

Steam in Arnold sterilizer for 45 minutes first day and again for 45 minutes the following morning.

The cream should be placed in refrigerator overnight following the first steaming. Remove chill the following morning before steaming the second time.

(b) *Milk-potato flour-asparagin mixture:* Into 3L sterile flask containing glass beads place the following:

Potato flour	37 grams
asparagin	3.6 grams

Mix well in dry state.

Add 556 cc. of milk. Mix well.

Place flask in boiling water bath and shake frequently for 10 minutes, then allow flask to remain in boiling water bath for 60 minutes longer with occasional shaking. This is prepared on the first day and refrigerated over night. The following morning, bring the mixture to room temperature and add 186 cc. of the cream-milk mixture after it has been steamed for second time and cooled.

(c) *Egg fluid:* Wash 52 average sized eggs with soap and water, rinse well and place in 70 per cent alcohol for 30 minutes. Transfer to sterile container to drain off the alcohol. Break the eggs and separate yolk into a sterile 2L beaker, until the 850 cc. mark is reached. Collect white in 600 cc. beaker until the 384 cc. mark is reached. Discard excess whites. Add the whites to the yolks and mix with the sterile heavy glass rod. Pour into 2L flask with glass beads and shake well. This thins the mixture and gets rid of viscid material.

(d) Pour total egg fluid into sterile 3L flask containing the cream-milk-potato mixture. Shake well.

(e) Add 24 cc. of 2 per cent malachite green oxalate and mix well.

(f) *Blending:* Pour mixture into the sterile Waring Blender in convenient amounts and run for 5 minutes. After each portion is blended pour into sterile 2L flask to allow separation of part of froth. As the froth separates pour fluid into the sterile dispensing burette where further separation of froth occurs in a few minutes.

(g) Dispense in 10 cc. amounts in sterile 1 oz. bottles.

(h) Inspissate at 82° to 88° for 1 hour.

(i) Incubate 72 hours for sterility test.

NOTE: Final medium should contain 3 to 3.5 per cent butter fat.



FIGURE 1: The two bottles on the left were specimens from patient J. P. inoculated 6-9-53 and read 7-6-53. The left bottle is the Lowenstein-Jensen medium and was recorded as a 1 plus growth. The other is the cream-egg medium and was recorded as 3 plus growth. The two bottles on the right are from patient H. M. inoculated 7-14-53 and read 8-15-53. The Lowenstein-Jensen medium was negative, the cream-egg medium has 13 colonies.

Experimental Report

The study will be reported in four phases viz:

(a) A comparison with the Lowenstein-Jensen medium for diagnostic value; (b) the comparative growths; (c) contamination possibilities; and (d) revival of certain smear-positive forms, negative on cultures.

The first will be given in Table I.

Gastric smears were not made because we feel the results contribute little worthwhile information due to the presence of saprophytes. Inoculation of the mediums were alternated throughout.

TABLE I

The results of the growth of 27 cultures with no growths, on one medium and one or more colonies on the other.

No.	Source	A. F. Bacilli on Conc. Smear	Colonies on C-E	Colonies on L-J
1.	Gastrics	Not done	0	1
2.	Gastrics	Not done	0	1
3.	Gastrics	Not done	0	1
4.	Gastrics	Not done	0	1
5.	Sputum	Negative	0	1
6.	Sputum	Negative	0	1
7.	Sputum	Negative	0	1
8.	Sputum	Negative	0	1
9.	Gastric	Not done	1	0
10.	Gastric	Not done	1	0
11.	Pus	Negative	1	0
12.	Sputum	Negative	1	0
13.	Sputum	Negative	1	0
14.	Sputum	Negative	1	0
15.	Sputum	Negative	1	0
16.	Sputum	Few	1	0
17.	Gastric	Not done	2	0
18.	Sputum	Negative	2	0
19.	Sputum	Few	2	0
20.	Sputum	Few	9	0
21.	Sputum	Negative	13	0
22.	Sputum	Negative	16	0
23.	Sputum	Negative	18	0
24.	Sputum	Negative	20	0
25.	Sputum	Moderate No.	1+	0
26.	Sputum	Few	1+	0
27.	Sputum	Negative	2+	0

Of these 27 cases where *one* medium was negative and the *other* positive, eight (29.6 per cent) were positive on the Lowenstein-Jensen medium whereas 19 (70.4 per cent) were positive on the cream-egg medium. Three of the cultures (25, 26, 27) were strongly positive with plus and double plus growths on the cream-egg medium and five similar to 20 to 24 inclusive had nine to 22 colonies each. Not one of the Lowenstein-Jensen cultures showed such difference.

The first 16 may well be explained on a basis of scanty distribution in the specimens as there were eight on each. The last 11 cannot be explained on any other basis than a superior enrichment of the cream-egg medium.

The next comparison was where there was a difference in growth on one or the other mediums. This feature will be shown in the next four

tables. The first of this group included cultures with a minimum of one colony on one medium and two to 20 on the other. The results are shown in Table II.

One specimen (No. 5) had a growth preponderance on the Lowenstein-Jensen medium whereas there were five with a preponderance of growth on the cream-egg medium (No. 8-12 inclusive). This group presented the same pattern as those in Table I.

The next group is a summary of 49 cultures where there was a minimum growth of two colonies on one medium with a maximum of 40 colonies on the other. The results will be lumped in one small table.

Of the 49 cultures 11 had the same number of colonies and 38 were different. Of 38 cultures showing a difference, 25 (51.1 per cent) showed a better growth on the cream-egg and 13 (26.5 per cent) a better growth on the Lowenstein-Jensen medium. There was almost double the efficiency of the cream-egg medium on these scantily positive specimens.

TABLE II

No.	Source	A. F. Bacilli on Cone. Smear	Colonies on C-E	Colonies on L-J
1.	Gastric	Not done	1	2
2.	Gastric	Not done	1	2
3.	Pus from knee	Negative	1	2
4.	Sputum	Negative	1	2
5.	Sputum	Negative	1	11
6.	Sputum	Negative	2	1
7.	Sputum	Negative	3	1
8.	Sputum	Negative	6	1
9.	Sputum	Negative	7	1
10.	Sputum	Not done	16	1
11.	Sputum	Few	18	1
12.	Sputum	Many	20	1
			77 Col.	26 Col.

The 85 cultures having only growths report in number of colonies and not including those in Table I shown by plus signs, was also grouped in a small table.

TABLE III

No. Colonies	Cultures Number Per Cent	Total colonies
		Number Per Cent
Same No. on both	11 (22.4)	62 (6.4)
More on "L-J"	13 (26.5)	382 (39.5)
More on "C-E"	25 (51.1)	523 (54.1)

TABLE IV

	Pos. on "C-E"	Pos. on "L-J"	% more on "C-E" than on "L-J"
Cultures	77 (90.6)	69 (81.0)	11.6
Colonies	761	493	54.3

TABLE V

No.	Source	A. F. Bacilli on Conc. Smear	"C-E"	"L-J"
1.	Sinus	Few	9 col.	1+
2.	Sputum	Moderate No.	40 col.	2+
3.	Sputum	Moderate No.	2+	4+
4.	Sputum	Moderate No.	3+	4+
5.	Sputum	Moderate No.	3+	4+
6.	Lung	Few	1+	4 col.
7.	Sputum	Few	1+	6 col.
8.	Sputum	Few	1+	15 col.
9.	Sputum	Negative	1+	16 col.
10.	Sputum	Few	2+	5 col.
11.	Sputum	Negative	2+	16 col.
12.	Sputum	Negative	4+	7 col.
13.	Sputum	Negative	2+	1+
14.	Sputum	Negative	2+	1+
15.	Sputum	Few	2+	1+
16.	Sputum	Moderate No.	2+	1+
17.	Sputum	Many	3+	1+
18.	Sputum	Few	3+	1+
19.	Sputum	Many	3+	1+
20.	Sputum	Few	3+	2+
21.	Sputum	Few	3+	2+
22-23	Sputum	2 cultures	4+	1+
24-26	Sputum	5 cultures	4+	2+
29-36	(1 gastric) (1 br. wash) (6 sputa)	8 cultures	4+	3+

Growth appeared on 77 (90.6 per cent) of the cream-egg medium and 69 (81.0 per cent) with the Lowenstein-Jensen medium. There was 11.6 per cent more positives on the cream-egg medium with a 54.3 per cent greater colony yield.

A record of comparable growths (expressed in the number of colonies) has been given in Tables II, III, and IV. Differences in 36 cultures with heavier growths on one or the other medium are tabulated in Table V.

In all 36 cultures, only 5 (13.9 per cent) showed better growth on the Lowenstein-Jensen medium than on the cream-egg medium, while 31 (86.1 per cent) cultures showed better growth on the cream-egg medium.

Up to this point the two media have been compared as to their *differences* in growth results. There were many, however, showing the same number of colonies on both media although almost invariably there were larger colonies on the cream-egg medium. In this group were six with one colony each, three with two colonies each and two with 25 colonies each—a total of 11. Of the growth having a 1 plus growth or better there were 11 each with 1 plus; eight each with 2 plus; four each with 3 plus, and 48 each with 4 plus growth—a total of 82 (42.0 per cent of all) having the same number of colonies or approximately the same amount of growth on both media.

The final summary of the growth comparisons on cultures of 195 specimens may be given as follows: There were 27 where one of the media produced growths, but not the other—eight for the Lowenstein-Jensen and 19 for the cream-egg medium—11 more than on the former with

eight having a preponderance of growth on the latter.

There were 86 cultures where there was only a difference in growth results—23 with more growth on the Lowenstein-Jensen medium and 63 with more on the cream-egg medium. Then, there were 82 where the growth was the same on both media.

By combining all figures for each medium in cultures from 195 specimens, it gives the Lowenstein-Jensen medium an advantage in 31 (15.9 per cent); the cream-egg medium an advantage in 82 (42.0 per cent) with 82 (42.0 per cent) where growths were equal. The net advantage, therefore, for the cream-egg medium is 26.1 per cent—5.6 per cent more positive specimens for tubercle bacilli and 20.5 per cent better growth.

While enrichment possibilities are markedly in favor of the cream-egg medium, the comparison is not complete without comparison of the possibilities of contamination.

Accordingly a comparison was made in 1091 specimens where there were 30 cream-egg bottles contaminated and only eight of the Lowenstein-Jensen medium a ratio of about 4 to 1 or 2.7 per cent to 0.7 per cent.

Of the 516 bottles in the incubator at this time five each are completely overgrown with contaminations. There are 12 (2.3 per cent) of the cream-egg medium partly contaminated and 5 (1.5 per cent) of the Lowenstein-Jensen medium partly contaminated. There is no doubt that the Lowenstein-Jensen medium is easier to prepare without risk of contamination than the cream-egg medium. In the whole series, however, no essential losses were encountered by either medium, since two bottles for each specimen are used and are recommended.

A check was made to see how many positive smear cases failed to grow. Of 519 specimens, one case on drug treatment about three months was repeatedly positive on smear but six cultures were negative. There were four cases with a moderate number of bacilli and two with numerous bacilli (a total of 25) that did not produce any growth. It would seem that an inhibiting factor was present in some of the cases that were negative on culture, particularly on the case with six positives with a moderate number of bacilli on the slide but which were uniformly negative.

Discussion

The advantage of the cream-egg medium over the modified Lowenstein medium would certainly be no less over the many other media that have been recommended. In the study reported above (8) an evaluation of some of the most commonly used medium was made, but none equalled the two used in this study and the cream-egg combination was then as now better than the Lowenstein-Jensen-Holmes medium.

After all other considerations are evaluated, the fact that the cream-egg combination is apparently the only one of all that will not only grow the human strain better, but it will also grow all bovine bacilli directly from bovine specimens. It may be considered a universal medium, therefore, for growing all mammalian and avian tubercle bacilli. It is more difficult to

prepare than other media, but we submit that it is worth the effort.

There is no doubt but some cultures were obtained that failed to grow on the reliable Lowenstein medium, but all of the acid fasts did not grow. There was some evidence in at least seven cases where a large number of bacilli in sputum failed to grow on culture indicating an inhibiting factor as a result of drug treatment. Not enough work has been done on pathological material to justify a statement but there were not many specimens containing large numbers of acid fast bacilli that have failed to grow. It is to be expected, however, that every bacillus in dying reaches and passes a stage when nothing can revive it.

It is not to be inferred that this is the last word in culture media. Other more delicate methods may supplant it in time. For the moment, however, it is the best we have tried. It may be that certain ingredients are not necessary, but until they are proved to be dispensable, they should be retained.

It should be pointed out also that this medium has its greatest usefulness in diagnosis. Synthetic media or media with "simple" formulas do not give comparable results where a diagnosis is desired.

The difficulty in making the cream-egg medium is more than other media but it is not much more difficult than the preparation of the Lowenstein-Jensen medium. It becomes a question of what price are we willing to pay for more positive specimens? It is still only about 5 per cent the cost of guinea pigs and will give results that are comparable.

The qualities of the cream-egg medium supply most needs for the growth of tubercle bacilli. It is high in egg yolk—an enriching ingredient of many substances used by tubercle bacilli; it contains only enough egg white to give the medium a firm body since too much albumen inhibits growth; it contains milk to give salt mixtures and protein; the cream gives fatty acids and glycerol; the potato is empirical but giving starch, salts, and proteins; and malachite green oxalate as an inhibitor of secondary micro-organisms.

Since the cream-egg medium is such a fine enriching mixture it is only to be expected that it will also grow contaminants better than other media. The main problem is to keep the contaminants at a minimum both in the specimen being examined and in the preparation of sterile glassware. Penicillin may be used to keep down contamination in grossly contaminated specimens but it is better to prepare the medium as free from contamination as possible before resorting to such aids.

SUMMARY

A comparison has been made between a cream-egg-potato mixture and the Lowenstein-Jensen-Holmes medium for isolating tubercle bacilli from septic material.

In 195 routine hospital specimens there were 11 (5.6 per cent) more positives on the cream-egg medium than on the Lowenstein-Jensen-Holmes medium. Some of these cultures were strongly (+ and++) positive.

There were in addition 63 more cultures that showed better growth on

the cream-egg medium than on the Lowenstein-Jensen-Holmes medium. Since 23 cultures showed better growth on the latter it leaves a net gain of 40 cultures (20.6 per cent) for the former.

There is an overall advantage, therefore, of (11+ 40 = 51) 26.5 per cent of the cream-egg medium over the Lowenstein-Jensen-Holmes medium.

There were a few positive specimens that failed to grow on culture where it seemed that an inhibiting factor had resulted from drug treatment.

Advantages and disadvantages of the cream-egg medium are discussed. The advantages are many and the disadvantages are duly compensated for, as there is no substitute for an increase in positive findings.

RESUMEN

Se ha hecho una comparación entre una mezcla de crema-huevo-patata y el medio de Loewenstein-Jensen-Holmes para aislar el bacilo de la tuberculosis del material séptico.

En 195 especímenes de rutina de hospital, hubo 11 (5.6 por ciento) más positivos en el medio de crema huevo que en el de Loewenstein-Jensen-Holmes. Algunos de estos cultivos fueron fuertemente positivos (+ y ++).

Además hubo 63 cultivos más que mostraron mejor crecimiento en el medio de crema-huevo que en el de Loewenstein-Jensen-Holmes.

Puesto que 23 cultivos mostraron mejor crecimiento en el último, queda una ganancia neta en favor del primer medio de 40 cultivos (20.6 por ciento).

Por tanto, hay una ventaja global de 11 más 40 o sean 51 (26.5 por ciento) por parte del medio de crema-huevo frente al de Loewenstein-Jensen-Holmes.

Hubo algunos pocos especímenes positivos que no crecieron en el cultivo en los que pareció haber un factor inhibiente que resultó de tratamiento con drogas.

Se discuten las ventajas y las desventajas del medio de crema-huevo. Las ventajas son muchas y las desventajas son compensadas debidamente, ya que no hay cosa que substituya al aumento de hallazgos positivos.

RESUME

Les auteurs ont fait une étude comparative d'un milieu comprenant un mélange de crème, d'oeufs, et de pomme de terre, et du milieu de Loewenstein-Jensen-Holmes, pour isoler les bacilles tuberculeux en partant de produits septiques.

Sur 195 produits provenant des examens courants de l'Hôpital, il y a eu 11 examens de plus (5,6%) qui furent positifs sur le milieu à la crème et aux oeufs, par comparaison au milieu de Lowenstein-Jensen-Holmes. Certaines de ces cultures furent même fortement positives.

En outre, il y eut 63 cultures qui, sur le milieu à la crème et à l'oeuf, donnèrent lieu à un développement supérieur à celui obtenu sur milieu de Lowenstein. Si l'on compte que 23 cultures donnèrent un développement supérieur sur ce dernier milieu, il en résulte un avantage très net pour le

milieu à la crème puisqu'il s'agit de 40 cultures, soit 20,6%. En comprenant l'ensemble, il y a un avantage de II + 40, soit 51, soit 26,5% en faveur du milieu à l'oeuf et à la crème.

Il y eut un certain nombre de produits qui s'étaient montrés positifs sur lames qui ne donnèrent pas lieu à une culture. Il semble qui s'est agi dans ce cas d'une inhibition due au traitement.

Les auteurs mettent en discussion les avantages et les inconvénients du milieu à la crème et aux oeufs. Les avantages sont considérables, et les inconvénients en sont nettement compensés car aucun argument ne peut être opposé à la notion de l'augmentation des cas positifs.

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Chronic Bronchitis—A Neglected Disease Entity*

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As a primary disease entity, chronic bronchitis is said to be rare and is often described as a problem of the elderly and aged.^{1,2} In the past it has rated little attention or importance as a pulmonary disease. One cannot, however, remain unimpressed by the number of chronic coughers whom one sees, not only as patients but as fellow workers and acquaintances. Many medical teachings leave the impression that study of such people with chronic cough usually will show them to have pulmonary tuberculosis, bronchiectasis or bronchogenic carcinoma. However, in the vast majority, investigation fails to disclose evidence of these important and time-honored entities. Instead, simple chronic bronchial irritation and inflammation appears in our experience to be by far the most common cause of the cough.

The importance of chronic bronchitis is not limited to its recognition as an etiological factor in the differential diagnosis of chronic cough. It is of great significance as a disease entity itself since we have found it to be the most common cause of pulmonary emphysema.

This is a study of 18 cases of chronic bronchitis. The incidence of the problem, clinical and pathological findings, as well as the important complications will be discussed.

Method of Study

A study was made to determine the causative mechanism of chronic cough in adult males who did not have evidence of pulmonary tuberculosis, bronchial asthma, chronic pneumonitis or bronchogenic carcinoma. The majority of patients with chronic pulmonary symptoms seen at this hospital do not have any of these entities. In the initial study 18 cases from among the many with long standing severe chronic cough were selected at random. It was reasoned that any pathological condition in the lungs or bronchi would be less likely overlooked by the means of study at our disposal in the severer cases and in addition information regarding the nature of the disease in its advanced form would be furnished. Work-up included history and physical examination, appropriate laboratory work, x-ray and fluoroscopic examination of the chest and electrocardiogram. An evaluation of degree of cough and amount of sputum was made. Bronchoscopy with bronchial biopsy and bronchograms were done on all cases. Studies of pulmonary function were carried out whenever feasible. The maximum breathing capacity was measured by means of a high velocity one-way flutter valve and a Douglas bag. The best of three attempts

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(30 seconds each) was used. The walking ventilation was calculated by collecting the expired air over a three-minute period while walking at a speed of 180 steps per minute (the specimen being collected by means of the high velocity and Douglas bag). The minute volume was calculated from air expired in the collecting apparatus over a six-minute period. The vital capacity was determined by means of a spirometer. From the information obtained in these studies, the air velocity index³ and walking index⁴ were calculated.

The finding of advanced degrees of emphysema in the group of patients under study led us to approach the problem from a second aspect. The bronchial trees of 20 cases who died with extensive pulmonary emphysema and who did not have tuberculosis, tumor or bronchial asthma were investigated by careful dissection and multiple sections. From the information gathered from both the clinical and post-mortem studies, it was hoped to establish the factors operating in the production of pulmonary emphysema.

Results of the Clinical Study of 18 Cases of Severe Chronic Coughers

1. Age: All were 50 to 69 years, except three who were between 40 and 50 years. All were males (veterans).
2. Duration of cough: Frequently the date of onset could not be remembered—most patients stated they had coughed for "years," 10 or more years being the rule.
3. Sputum: All raised sputum. In 13 the amount was less than half a cup. Five averaged more than one cup per day. Hemoptysis was present in four. The amount of blood coughed was considerable in amount in two during an episode which prompted hospitalization. The bleeding stopped spontaneously in each.
4. Agents responsible for cough: (a) Previous known pulmonary infection: pneumonia occurred in three—in one of these, however, chronic cough antedated pneumonia. (b) Exposure to industrial irritants—none in this series. In other types of communities, such as those with mining or quarry work as major industries, this factor could be important. (c) Inhalation of tobacco smoke—all smoked from one to three packages of cigarettes per day.
5. Other respiratory symptoms: Dyspnea of varying degrees were noted in 15.
6. Physical examination of the chest showed increase in the anteroposterior diameter in 16. The lungs showed rhonchi and basal rales in 18 and a wheeze was noted in six. Right heart failure due to cor pulmonale was seen in three.
7. Laboratory findings: The sputum contained few to many pus cells. Bacteriological study showed usual inhabitants of upper respiratory tree, Neisseria, Strep. viridans, Aerobacter aerogenes, proteus. A few had sputum in which D. pneumonia was the predominant organism. Blood counts showed normal white blood cells and differential. The hematocrit was over 50 in six and over 60 in two, both of whom had cor pulmonale. Blood chem-

istries were measured in eight of whom three showed respiratory acidosis.

8. Electrocardiogram showed right ventricular strain in two: In others the tracings were normal. Marked clockwise rotation was a common finding.
9. Chest X-Ray: In nine, increased radiability of the lung fields was reported. The diaphragms tended to be depressed. The heart size was enlarged in two.
10. Bronchoscopy: Reddening of the mucosa and increased secretions were noted. No complications occurred from the procedure. Bronchograms failed to show evidence of bronchiectasis in any case. Bronchial biopsies disclosed chronic bronchitis in all.
11. Ventilatory studies (Table 1): The maximum breathing capacity (MBC) showed considerable reduction in most instances. Extremely low values were seen in eight. The vital capacities were reduced to a much lesser extent with the result that the air velocity indices were uniformly less than one. Reduction in MBC of greater degree than that of the vital capacity has been shown to indicate obstruction to flow of air and is characteristically seen in bronchial asthma, bronchiectasis and pulmonary emphysema. Loss of pulmonary elasticity, bronchiolar narrowing due to secretions, mucosal thickening and inflammation, air trapping and the chest deformity all contribute to reduce the MBC in pulmonary emphysema. The low air velocity indices confirm in our cases the clinical impression of emphysema and, in addition, serve as an index of the severity. The walking indices indicated serious impairment in breathing reserve in 10 of the 13 cases in which

TABLE 1 - VENTILATORY STUDIES IN CHRONIC BRONCHITIS

Case	MBC	Predicted MBC	%Predicted MBC	Vital Capacity	Predicted VC	%Predicted VC	AIR Velocity Index	Walking Vmt. L/M	Walking Index
	L/M	L/M	L/M	L	L	%		L/M	
1. W.Y.	.61	125	49	2.9	4.0	72	.68	23	.39
2. R.G.	.38	82	39	2.6	3.4	82	.47	23	.22
3. G.S.	.70	106	70	3.0	3.4	88	.79	12	.17
4. G. F.	.50	88	57	2.8	3.8	66	.65	—	—
5. R.B.	.66	132	60	4.0	3.9	102	.50	—	—
6. R.A.G.	.76	103	72	3.2	3.8	86	.86	17	.23
7. F.J.	.75	111	68	—	3.8	—	—	—	—
8. F.R.	.96	115	82	3.6	3.6	96	.87	19	.20
9. J.Y.	.26	101	25	3.2	3.3	97	.24	16	.67
10. R.J.	.30	85	35	2.4	3.3	73	.48	14	.47
11. G.G.	.33	108	31	2.6	3.1	86	.57	22	.67
12. R.R.	.16	106	36	2.2	3.5	63	.41	16	.61
13. A.K.	.56	104	53	3.4	3.5	97	.26	18	.69
14. J.K.	.30	113	27	2.4	3.7	65	.26	—	—
15. R.G.	.96	102	92	3.6	3.8	95	.97	—	—
16. P.F.	.56	112	50	2.4	3.4	71	.70	23	.41
17. R.P.	.20	66	37	2.1	3.3	62	.43	15	.62
18. J.H.	.41	105	39	3.4	3.4	100	.79	19	.40

a walking ventilation was done, and in one other, (Case 14), the walking ventilation could not be obtained satisfactorily due to dyspnea. Timed vital capacities were done in a few instances and showed the characteristic delay seen in emphysema.

Findings In 20 Autopsy Cases of Emphysema

Post-mortem examination of the bronchial tree and pulmonary parenchyma of 20 cases with autopsy evidence of advanced emphysema was carried out. Those with tumor, bronchial asthma, and tuberculosis were excluded. The object of the study was to determine which pathologic entities were associated with the finding of emphysema at autopsy. In all 20 chronic bronchitis was found to be present. In addition, bronchiectasis was found in two. Evidence of cor pulmonale was present in five.

Twenty cases of Emphysema at Autopsy

Disease	Present		Absent	
	No. per cent		No. per cent	
Chronic bronchitis	20	100	0	0
Bronchiectasis	2	10	18	90
Cor Pulmonale	5	25	15	75

Discussion

The clinical sequence of events appears with almost monotonous similarity in these cases. The onset of the problem is insidious, usually in early adult life. Cough is the only symptom at first. Characteristically, this is especially noted after arising in the morning. At that time a paroxysm of coughing occurs often with the raising of some tenacious, whitish, mucoid sputum which has collected in the bronchial tree during sleep. During the rest of the day cough is usually minimal and often not particularly noticed by the patient himself. He feels well and rarely seeks medical attention then. A few consult family physicians and may be referred for a chest x-ray film. This is invariably "negative" or shows "increased broncho-vascular markings." Satisfied with assurance that there is no "T.B.," but only "bronchial catarrh" or "just a cigarette cough," as a rule the patient continues in his previous status without attaching any serious importance to the cough.

With the passage of time, often years, the cough gradually increases so that it is noticeable not only in the morning, but also during the rest of the day. It is characteristically worse during intercurrent acute upper respiratory infections which are apt to last longer than usual. Damp, cold weather also aggravates the symptom. Dyspnea may appear for the first time heralding the presence of significant pulmonary emphysema. In advanced cases, frank pulmonary insufficiency with or without cor pulmonale is seen.

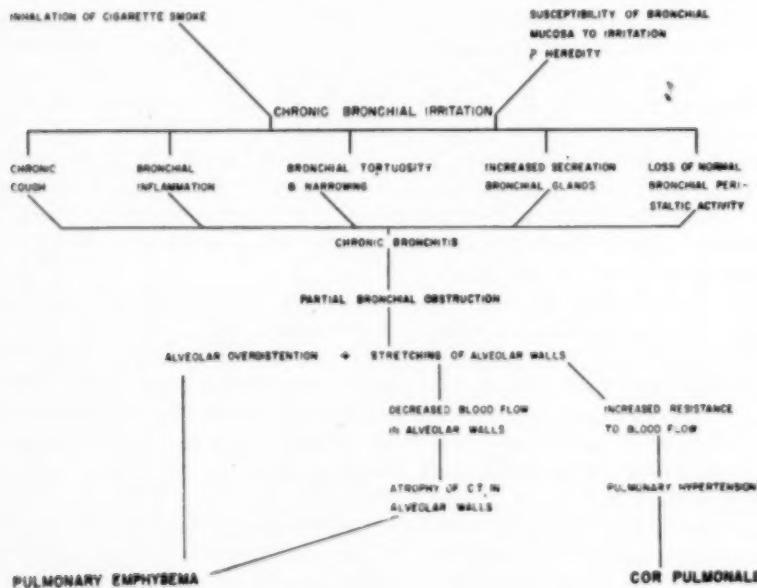
The cardinal feature of the problem clearly seems to be chronic bronchial irritation, evidenced by chronic cough. Bronchoscopic and pathologic studies confirm the inflammatory lesion in the bronchial tree. In con-

sidering the basic mechanism, it seems essential to determine the etiologic factors which produce the bronchial irritation. Known agents in the production of bronchitis include specific pulmonary infections such as tuberculosis and fungus diseases, structural alterations such as bronchiectasis, bronchial obstruction from tumor, foreign body and external pressure of nodes and aneurysms, and allergy in the form of bronchial asthma. In addition, inhalation of irritating substances, industrial and others, chiefly tobacco, may be responsible for the bronchitis.

Although any of these multiple agents may act as sources of chronic bronchial irritation, it is only an occasional case of chronic cough that we find the bronchitis attributable to any agent other than inhalation of cigarette smoke. This is not to imply that patients with chronic cough should not be investigated for other specific pulmonary disease, that any individual case should be labeled primary chronic bronchitis without study. It is merely that in our experience, study of the vast majority of chronic coughers by careful history for prior specific pulmonary infections or exposure to industrial irritants, by physical and roentgen studies of the chest including bronchoscopy and bronchography, by sputum studies including cytology, discloses evidence of no other agent than inhalation of cigarette smoke as the irritating substance.

A recent report emphasized that certain persons are more susceptible to irritation from tobacco smoke; that cough and wheezing may be produced in these individuals by as few as five or six cigarettes per day.⁵

COMMON MECHANISM OF DEVELOPMENT OF PULMONARY EMPHYSEMA



These symptoms were not considered to be primarily an allergy to tobacco (no allergic background in the patients and negative skin tests to tobacco), but rather that they were related to the direct irritating response of bronchial mucosa sensitive to substances in the smoke. A similar reaction of the larynx has also been described.⁶ Others also note the high incidence of inhalation of cigarettes as the etiologic agent responsible for chronic cough.⁷ As further evidence that this is the agent of irritation, we observe that when smoking is discontinued the cough usually disappears and is always reduced in severity. In recent years considerable statistical evidence has accumulated to show an association of cigarette smoking and bronchogenic carcinoma.^{8, 9} In our experience, the association of previous long standing chronic bronchitis with bronchogenic carcinoma has also been extremely high. In view of the finding of cigarette smoking as the principal agent in the production of chronic bronchitis, this may further clarify the relationship between smoking and bronchogenic carcinoma. This will be reported at another time.¹⁰

The mechanism whereby chronic bronchitis leads to the development of pulmonary emphysema appears to be related to the diffuse bronchiolar obstruction seen in the disease. Histologic study shows clear evidence of diffuse involvement of bronchioles in all lobes of the lungs with inflammation, narrowing, elongation and tortuosity.¹¹ Loss of normal bronchial peristaltic waves whereby secretions are removed from the bronchi have been shown to be absent.¹² Excessive secretions from the mucous glands¹³ and cough act as further dynamic factors to obstruct the bronchial tree.

The partial obstruction of the air passages to the alveolar sacs results in their overdistention. This overdistention with trapped air compresses and stretches the alveolar walls impeding the flow of blood to the alveoli and to the walls. Atrophy of the elastic connective tissue elements of the walls results in loss of elasticity of the lung. The impeded flow of blood in the alveolar walls also results in pulmonary hypertension. Cor pulmonale may follow.

In the case of bronchitis from tobacco irritation, diffuse bronchial involvement seems probable because of the nature of dispersion of the agent in the pulmonary tree (inhalation of cigarette smoke). Pathologic material taken by biopsy from various bronchi showed no selective findings. Similarly, autopsy findings indicate a diffuse process. The possibility that focal trigger areas of local bronchial obstruction also play an important role in the development of generalized pulmonary emphysema through autonomic reflex pulmonary arterial and bronchial spasm is emphasized by others.⁷ In addition, the possibility that circulatory occlusive changes of the bronchial arteries play a significant role in the production of lung atrophy has been suggested.¹⁴

SUMMARY

1. The majority of adult males seen by us with chronic cough do not have tumor, tuberculosis, bronchial asthma, bronchiectasis or chronic pneumonitis, but rather chronic bronchitis.

2. A clinical study of 18 such coughers with chronic bronchitis is presented.

3. Inhalation of cigarette smoke was found to be the common agent in the production of chronic bronchitis. No other cause for the cough was demonstrated.

4. All showed evidence of pulmonary emphysema, usually of severe degree in long standing cases.

5. A study of 20 cases with autopsy evidence of pulmonary emphysema and without tuberculosis, tumor, or asthma, disclosed chronic bronchitis in all and the only associated bronchial disease in 18. Bronchiectasis was found in two cases.

6. It is felt that chronic bronchitis is the commonest cause of pulmonary emphysema. Mechanisms whereby this takes place are discussed.

7. A relationship between chronic bronchitis and bronchogenic carcinoma is alluded to.

RESUMEN

1. La mayoría de los adultos del sexo masculino con tos crónica no tiene tumor, tuberculosis, asma bronquial, bronquiectasia o neumonitis crónica, sino más bien bronquitis crónica.

2. Un estudio clínico de 18 tosedores con bronquitis crónica,-se presenta.

3. La inhalación de humo de cigarrillo se encontró que era el agente más común en la producción de la bronquitis crónica. (No se encontró otra causa de la tos).

4. Todos mostraron evidencias de enfisema pulmonar, generalmente severo en caso de larga duración.

5. En el estudio de 20 casos con evidencias a la autopsia de tener enfisema pulmonar y sin tuberculosis, tumor, o asma, se encontró sólo asociada la bronquitis crónica en 18 y sólo en dos bronquiectasia.

6. Se cree que la bronquitis crónica es la causa más común del enfisema. Los mecanismos que intervienen se discuten.

7. Se hace alusión a una relación entre la bronquitis crónica y el carcinoma bronquiogénico.

RESUME

1. La majorité des adultes du sexe masculin qui ont été examinés par les auteurs n'étaient atteints ni de cancer, ni de tuberculose, ni d'asthme, ni de bronchiectasie ou de pneumonie chronique, mais plutôt de bronchite chronique.

2. Les auteurs présentent l'étude de 18 de ces toussieurs habituels, atteints de bronchite chronique.

3. La cause habituelle de cette bronchite chronique semble être l'inhalation de fumée de cigarette. On ne put mettre en évidence aucune autre cause de cette toux.

4. Tous les malades avaient un emphysème pulmonaire qui, généralement, était très important lorsque la maladie évoluait depuis longtemps.

5. Chez 20 malades pour lesquels l'autopsie aux en évidence l'existence d'emphysème, on ne put constater ni tuberculose, ni cancer, ni asthme, mais

chez tous une bronchite chronique et dans 18 cas une affection bronchique associée. Chez deux malades, il existe une dilatation des bronches.

6. Les auteurs estiment que la bronchite chronique est la cause la plus commune d'emphysème pulmonaire. Ils mettent en discussion le mécanisme de cette constatation.

7. Ils font allusion à la relation qui unit la bronchite chronique et le cancer des bronches.

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County Wide Tuberculin Testing*

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During the past 25 years tuberculin testing surveys have been used extensively and effectively in Minnesota's fight against tuberculosis. The program started in the schools. S. A. Slater, Southwestern Minnesota Sanatorium, Worthington reported testing 1,654 rural children in 1924. The idea spread slowly at first but soon gained momentum. Now hundreds of communities in this state have routine yearly testing of their school population. Recently tuberculin testing has in certain sections of Minnesota been extended to include the entire population.

When we first started the percentage of the school enrollment taking advantage of the test was small, 60 or 70 per cent was a good response. The percentage of reactors, on the other hand, was high, 15 to 25 or even up to 40 per cent in some places.

We soon learned that one mass survey of a school was of little value in furthering the cause of tuberculosis control. Surveys had to be done at regular and frequent intervals to get maximum cooperation and maximum effect. Offering the test to the whole enrollment every other year or to alternate grades every year has proved an effective measure, first, in protecting children from exposure to tuberculosis, and secondly, in maintaining in the community a high level of education on the facts of tuberculosis, its epidemiology, prevention and cure.

We also learned the importance of reaching as close to 100 per cent as possible. This was brought out tragically in many schools. For example in one small high school where one contagious case missed caused 93 per cent of the freshman class and 85 per cent of the rest of the high school to become reactors to tuberculin.

Awarding of certificates by the American School Health Association to schools meeting high standards of cooperation in the testing program has helped immeasurably. For instance, in the four counties served by the Riverside Sanatorium where regular surveys have been done for more than 20 years, 95 per cent or more of the total school enrollment of the four counties have been tested every other year for over 10 years, and all reactors, new and previously known, have had film inspections of their chests.¹

Perhaps the first adult group to be tested regularly and reactors x-rayed at least every two years has been the school personnel including teachers, janitors, bus drivers, cooks, secretaries, etc. Here also we learned the importance of this phase of the work by tragic instances of high percentages of reactors among the children due to an infective teacher, cook, or bus driver. We have many such instances on record.²

*Read before the Mississippi Valley Conference on Tuberculosis, October 16, 1953, Minneapolis, Minnesota.

From Riverside Sanatorium, Granite Falls, Minnesota.

Here also we were helped by awarding of certificates, since no school can receive one unless 100 per cent of its personnel is checked regularly by test and x-ray, yearly if possible or at least every two years. Minnesota has 1,500 schools which have received such certificates.

The testing of school children and of school personnel is not an isolated event in the community. If the survey is done correctly it entails the checking of the family and close associates of each reactor. It also implies reminding every known tuberculosis contact and known tuberculin reactor, in or out of school, that it is again time for regular x-ray film check-up. Thus, if school surveys are done regularly and well, a valuable fund of epidemiological facts about the whole community can thereby be obtained and used in the effective fight for tuberculosis control and eventual eradication.

In the many hundred communities where school testing is an established routine, these have been continued and requested even after mobile x-ray surveys were available. Public health nurses have found that among the school population, a testing survey gives them more information and the basis for more complete follow-up than x-ray surveys alone.

The step from school testing to community-wide testing has been a natural, although a rather considerable one. Twenty some years ago when school testing started it was not uncommon to find active cases among the children, especially in the high school groups. Patients in our sanatoria were then mostly young people, teen agers and young adults. The percentage of reactors in our schools was 15 to 25 or more in some instances. But as the on-coming generations were more and more protected from contact with contagious tuberculosis, the age of the patient suffering from the disease advanced. Now, in many of our counties tuberculosis has become a disease of middle and even old age. Findings in our schools have decreased. This fact led to considering the extension of testing surveys to the entire population, especially in low death rate counties.

The first tuberculin testing survey on a county-wide basis in Minnesota was begun in Meeker County in the spring of 1941. This was conducted by local physicians who administered tuberculin tests, read the x-ray films, and completed examinations without charge to individuals or any organization. The population of the county was then about 16,000. After 10,733 citizens of all ages had responded, it was necessary to discontinue the demonstration because of exigencies of war. Of the 10,733 who were tested with tuberculin, 2,445 (22.8 per cent) reacted. Of this number, 2,031 had x-ray inspection of the chest. The remaining 414 were scheduled when the demonstration had to be closed. Among the 2,031 reactors who had x-ray film inspection, 16 presented shadow-casting lesions which were proved to represent clinical tuberculosis. Thirteen of them were sent to sanatoriums and the remaining three were treated at home. Although this survey was only about two-thirds completed, it resulted in deep and sustained interest of the public and professional workers with fine subsequent accomplishments.

In 1946 the Minnesota State Medical Association Committee on Tuberculosis of which Dr. J. A. Myers was chairman, published a report entitled, "An Ideal Tuberculosis Case Finding Program." The committee recommended community wide or county wide tuberculin testing, to be followed by chest x-ray films of all reactors. Reactors should thereafter be x-rayed at least once a year and non-reactors retested with tuberculin every three years.

In 1951, county wide testing was again undertaken, this time under the joint sponsorship of the Minnesota Tuberculosis and Health Association and the Southwestern Minnesota Sanatorium district and medical societies.

The first selected for this project was Lincoln County. Under the leadership of Dr. Alfred Vadheim of Tyler, this county had first inaugurated school testing surveys and had been the first county to be accredited for tuberculosis control in human beings. It is definitely in the low tuberculosis death rate bracket.

It is a small county with a predominantly rural population, numbering 10,150 at the last census. It comprises six villages, the largest of which is Tyler with a population of 1,121.

Testing in this county was done by the local physicians who donated their services. Volunteer workers briefed at a county wide mass meeting canvassed and registered the whole population. Testing was done more or less simultaneously, at various centers, and so was completed in a short time. An x-ray film of reactors was taken by the State Board of Health mobile unit. Follow-up 14 x 17 x-rays were taken at Southwestern Minnesota Sanatorium and also by local physicians. Seventy-one per cent of the available population responded.

Although the county has a history of low tuberculosis morbidity as well as mortality, 30 per cent of the adults tested were reactors. The school children had 2.4 per cent and the total population 20 per cent. There was a steady rise in infection rate from 15 per cent in the 21 to 30 year group, to a little over 50 per cent in the 60 to 80 year group.

Lyon County, adjacent to Lincoln, was the next chosen for county wide testing. Its population is twice as large as that of Lincoln County and, although largely rural, does have some industrial workers and a larger percentage of urban as opposed to rural residents. Its county seat, Marshall, numbers 5,923. Tracy, the second largest town, 3,020. Lyon as well as Lincoln has had a low tuberculosis death rate. (The latest figure is 2.7 per 100,000 population).

Organization of the county for testing was somewhat different than for Lincoln County. Instead of one county wide mass meeting, each of the seven different towns held their own. A steering committee, consisting of Dr. M. H. Valentine of Tracy, president of the County Tuberculosis and Health Association, the superintendents of schools and representatives of the State Tuberculosis and Health Association coordinated the work for the whole county. Here again, volunteers canvassed and registered the population. Newspapers, radio-stations, various organizations and schools joined in all out publicity and educational campaign.

In this county testing and reading of tests were done by one person. This assured uniformity of administration and interpretation of the tests. It also made it possible to allocate more hours daily to the program in each locality. The main disadvantage was that the survey had to extend over a period of weeks.

The total number of persons reached was 14,177. This includes 510 who were not tested because they were previously known reactors and reported for x-ray films only. This was estimated to be about 79 per cent of the available population.

Reaction percentages were as follows:

	Per Cent
School Children	4.08
Adult males	37.6
Adult females	29.3
Percentage for the total population	22.4

The increase in reaction percentage with age is shown by the following figures and graph.

TABLE I
MEN

Ages	No. Tested	No. Reactors	Per cent
10-19	124	20	16.1
20-29	649	164	25.28
30-39	1155	323	38.8
40-49	888	356	40.0
50-59	574	285	47.7
60-69	396	235	59.3
70-79	163	89	54.6
80-89	31	14	45.1

WOMEN

Ages	No. Tested	No. Reactors	Per cent
10-19	177	26	14.68
20-29	989	177	17.9
30-39	1218	250	20.52
40-49	927	320	34.41
50-59	648	286	44.1
60-69	411	209	50.8
70-79	156	80	51.2
80-89	34	12	35.2

CHILDREN

	Total Tested	Reactors This Year	Total Reactors	Per Cent Total Reactors
Pre-School	222	2	3	1.35
1st-6th	2700	66	73	2.70
7th-9th	1169	56	59	5.04
10th-11th	660	42	50	7.57
12th	274	18	20	7.29
Grand Total	5025	184	205	4.08

The rapid rise in the reaction percentage among men between the ages of 20 and 45 as opposed to the much slower increase in the same reaction percentage in women commands attention (Table I and Figure 1). Men's occupations bring them in contact with many more people than do women's which probably accounts for part of the difference. The rest may be due to contacts made over seas during war time service. We asked as many young men as possible about their war time years. Many of them who had been non reactors in their senior year in high school and had gone from high school to the armed forces and were now back in civilian life did show reactions to tuberculin. However, our figures are too incomplete

to quote. We do think that this is an important group to reach in a testing survey. In any future county wide program questions on service in the armed forces should be included on the registration card.

In a study of occupations (Figure 2), reaction percentages were found to be as follows:

Retired	54.91
Business	47.63
Unskilled Labor	43.56
Skilled Labor	42.99
Professional	39.39
Public Service	38.51
Teachers & Superintendents	38.28
School Personnel	36.36
Food Handlers	34.00
Housewives	30.46
Farmers	30.08
Office Workers	29.68

See graph.

The reaction percentage in housewives would probably be the lowest if this group did not include women from 65 to 80 and above. The housewife never lists herself as "retired." The office workers listing was made up largely of young single women.

Reactor percentages arranged with reference to the birth place of the reactors show the foreign born group with a definitely higher infection rate than those born in Lyon County, in the rest of Minnesota, or in the United States exclusive of Minnesota (Figure 3).

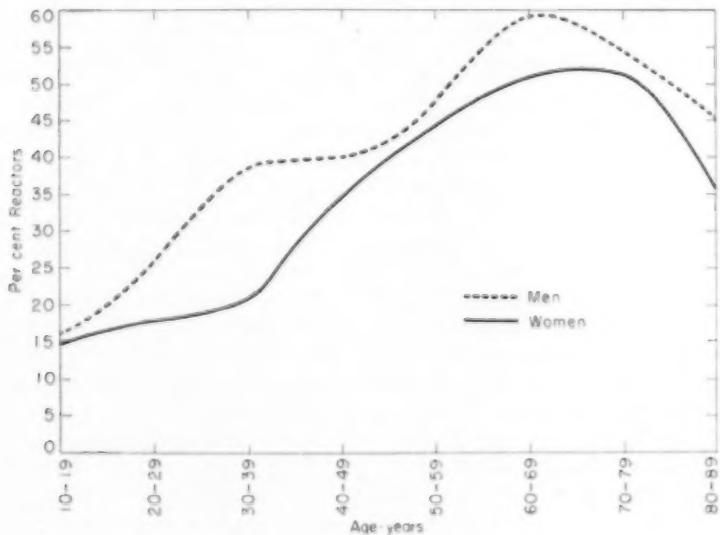


FIGURE 1

X-Ray Films of Chests of Reactors

A Minnesota Department of Health mobile x-ray unit spent one and one-half weeks in the county to make photofluograms of the chests of reactors. A total of 3,050 films was taken.

The following reports were received from the Health Department:

Possible Tuberculosis findings needing further study	70
Essentially negative but showing calcification	113
Emphysema or pleural changes	25
Cardiac and other non-tuberculous findings	39
Unsatisfactory films	36

Persons with cardiac or non-tuberculous findings were referred to their family physician. Those who showed need of follow-up for possible tuberculosis received letters wishing them to take advantage of a 14 x 17 chest x-ray film at Southwestern Minnesota Sanatorium, Worthington.

Dr. Slater's report on 122 x-ray films taken at the sanatorium is as follows:

Need for further intensive study.	
Left lung completely obscured and trachea pulled over to one side	1
Showed extensive fibrosis in one or both lungs	4
Showed shadows that demanded further study	4
Were apparently negative	63
Film showed no evidence of active pathology.	
Recheck in a few months advised	50
Thoracoplasty	1

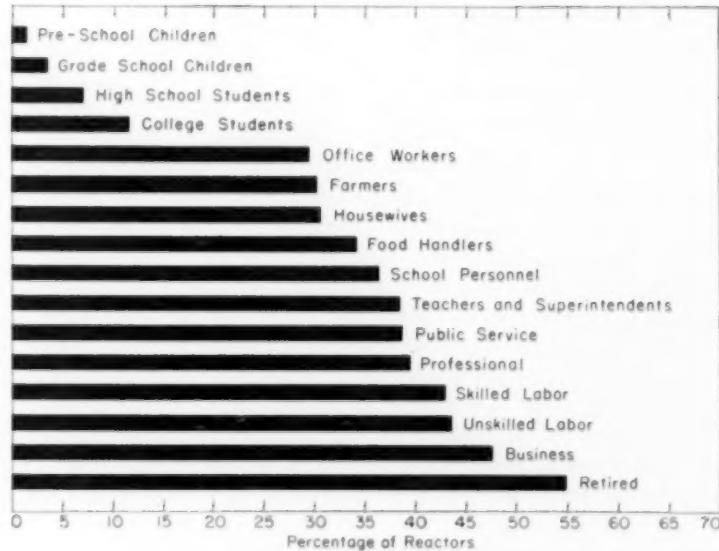


FIGURE 2

Many of the reactors chose to skip the mobile unit and went directly to the sanatorium or their private physicians for 14" x 17" films. Reports of films taken by the family physician are not complete at this time. Lists of reactors were sent to their own physicians and an effort is being made to reach those few who did not respond and remind them of the importance of this follow-up procedure.

It is our opinion that no county-wide testing survey can be successfully carried out without having been preceded by a complete and continuous school tuberculin testing survey program. The latter is an excellent educational factor in the community and a good index of the efficacy of the tuberculosis control program. Any increase over normal of the percentage of reactors indicates the need for more intensive work in search of the unknown infective agents.

If county testing seems to be too ambitious a program, it is our opinion that the inclusion of World War II and Korean Veterans in a school testing survey would give vital information for future control of tuberculosis. Reaching food handlers also is a good prevention measure. The ideal program, however, is 100 per cent county testing with regular x-ray film check-ups of reactors. This type of survey gives some very important information. In a county with low tuberculosis death rate and low morbidity one third of the adult population shows evidence of contact with tuberculosis at some time in their lives. When we first started testing school children 23 years ago we found schools with that high a reaction percentage. Now the same schools rarely show as high as 5 per cent reactors. Can we hope to achieve the same results for the whole county? It is a big undertaking but not impossible. This is the goal toward which we should work.

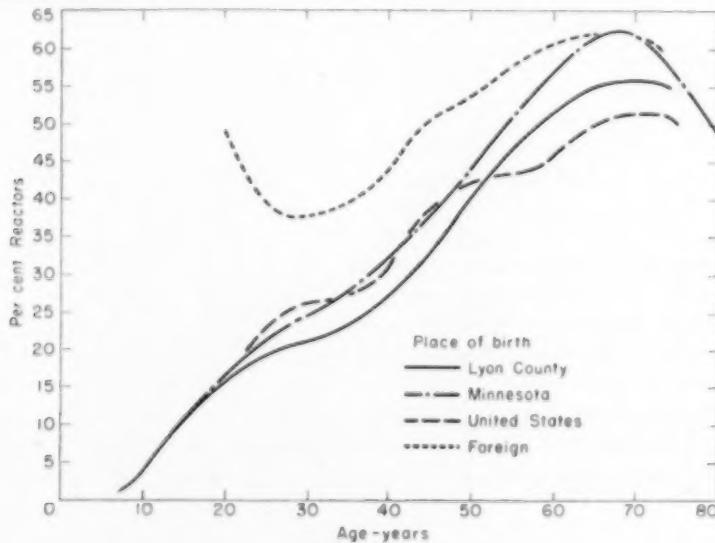


FIGURE 3

SUMMARY

1. County-wide tuberculin testing of people of all ages is the only procedure by which one can locate those who harbor tubercle bacilli. It is only persons in whom these organisms reside that now have, or subsequently develop, clinical tuberculosis. By finding all of these persons with the tuberculin test and examining them periodically, one is able to detect chronic evolving lesions many of which are sure to develop before they produce symptoms or are contagious. Since tuberculin reactors have usually been in contact with persons who have contagious disease it is often possible to find the sources of infection among their adult associates.

With these facts definitely established, we started routine tuberculin testing, first in the schools, more than 20 years ago. This was thought to be the best way to inform the citizenry of the value of the tuberculin test to everyone regardless of age. Through actual participation in the program, children, school personnel, and, indirectly, parents and the entire community became familiar with the procedure and recognized it as the most refined method of combating tuberculosis.

Thus, the stage was set for testing people of all ages on a county-wide basis, retesting the non-reactors periodically, and making immediate, and later periodic examinations of reactors on the first testing or those who subsequently become so.

County-wide tuberculin testing is now in progress in Minnesota, and we are reporting especially on such a survey recently conducted in Lyon county.

About 79 per cent (14,177) of the total population responded. Four per cent of the school children reacted, and this was true of 37.6 per cent of adult males and 29.3 per cent of adult females. Of the total population, 22.4 per cent were found to harbor tubercle bacilli through the tuberculin reaction. Thus, we have found where the tubercle bacilli in this county reside. It only remains to use well known methods to prevent the hosts of these organisms from spreading them to other people and animals.

RESUMEN

1. El único procedimiento por el cual se pueden localizar las personas de todas las edades que alojan bacilos de tuberculosis en su organismo, es por la prueba tuberculínica abarcando toda la comunidad. Sólo en las personas que tienen esos bacilos en su organismo es que la tuberculosis se desarrolla actualmente o se desarrollará en el futuro. Encontrando todas estas personas y examinándolas periódicamente está uno capacitado para descubrir lesiones evolutivas que seguramente muchas deellas se desarrollarán y producirán síntomas o se descubrirán antes de que sean contagiosas. Puesto que la reacción tuberculínica se presenta en los que habitualmente han estado en contacto con personas contagiosas es a menudo posible encontrar las fuentes de infección entre los adultos que con ellas se asocian.

Sobre estos hechos definitivamente establecidos, empezamos a hacer-

pruebas de tuberculina sistemáticamente en las escuelas desde hace 20 años. Nos pareció que esta es la mejor manera de informar a la comunidad del valor de la reacción tuberculínica en cualquiera edad. Por la participación en el programa de los niños, el personal escolar, e indirectamente los parientes, toda la comunidad se familiarizó con el procedimiento y lo reconocieron como el método más refinado para luchar contra la tuberculosis.

Así se hicieron arreglos para hacer las pruebas en las personas de todo el país volviendo a probar a los negativos periódicamente y examinando después a los positivos a la primera o a ulteriores pruebas.

Actualmente, se lleva a cabo ese proyecto en Minnesota y estamos refiriendo el estudio hecho recientemente en el condado de Lyon.

Aproximadamente 79 por ciento (14.177) del total de la población respondieron. Cuatro por ciento de los escolares reaccionaron así como 37.6 por ciento de los adultos hombres y 29.3 por ciento de las mujeres adultas. De la población total 22.4 por ciento se encontraron que tenían bacilos tuberculosos en su organismo de acuerdo con la reacción tuberculínica. Así hemos encontrado donde residían los bacilos tuberculosos en este condado. Sólo falta hacer uso de métodos bien conocidos para evitar que estos organismos se diseminen entre otros seres humanos o animales a partir de los sujetos que los hospedan.

RESUME

La recherche de l'allergie tuberculinaire des individus de tous âges, étendue dans toute une région, est le seul moyen de connaître ceux qui hébergent des bâcilles de Koch. La tuberculose-maladie ne peut apparaître que chez ceux qui sont déjà atteints par l'infection bacillaire, soit au moment où l'on découvre cette infection, soit plus tard. En repérant toutes ces personnes grâce à la recherche de l'allergie tuberculinaire et en les examinant périodiquement, il est possible de mettre en évidence des lésions à leur début, dont beaucoup sont visibles avant toute symptomatologie et avant de devenir contagieuses. Étant donné que les individus dont les réactions tuberculaires sont positives ont été habituellement en contact avec des personnes atteintes de tuberculose contagieuse, il est possible de retrouver de cette façon les sources de l'infection parmi les adultes qu'ils fréquentent.

Ces faits étant incontestablement établis, les auteurs commencèrent la recherche systématique des réactions tuberculaires, il y a plus de 20 ans, d'abord dans les écoles. Il apparut que c'était là le meilleur moyen de faire comprendre à tous la valeur des réactions tuberculaires pratiquées quel que soit l'âge. En prenant part à cette action, les enfants, le personnel scolaire, et indirectement les parents et tout l'ensemble de leurs fréquentations, se familiarisèrent avec le procédé et reconnurent qu'il s'agissait de la méthode la plus perfectionnée de lutte contre la tuberculose.

C'est alors qu'il fut décidé de rechercher les tests tuberculaires chez les individus de tous âges dans une région déterminée. Périodiquement,

on refit cette recherche chez ceux qui n'étaient pas allergiques. Des examens complets furent faits dès la première constatation d'une cuti-réaction positive et on refit ces examens périodiquement. Il en était de même lorsqu'on surprenait un virage de réaction tuberculinique. La recherche des réactions tuberculiniques d'un secteur géographique déterminé s'est étendue maintenant à tout le Minnesota, et les auteurs rapportent plus spécialement les résultats d'un examen systématique qui a été récemment poursuivi dans la région de Lyon.

Environ 79% (14.177) de l'ensemble de la population répondirent à la demande d'examen. Parmi les enfants des écoles, 4% eurent des réactions positives, et chez les adultes, les chiffres furent de 37,6% pour les hommes adultes, et de 29,3% pour les femmes. Sur l'ensemble de la population, en se basant sur les réactions tuberculiniques, on peut conclure que 22,4% des individus étaient porteurs de bacilles. Dans cette région les auteurs purent délimiter les zones du pays où se trouvaient les bacilles tuberculeux. Il ne reste plus maintenant qu'à utiliser les méthodes usuelles pour empêcher ceux qui hébergent les microbes de les transmettre à d'autres personnes ou aux animaux.

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The Rationale of Emphasis on Tuberculin Testing in a Tuberculosis Control Program

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From three to five million persons die of tuberculosis every year throughout the world. It is estimated that some 50 million people have the disease, and are transmitting the organisms to other people.¹ The disease has been a major scourge of mankind through all recorded history, but only since the last part of the 19th century has it been clear that it is a contagious disease. In Western civilization the death rate has been declining since 1870—that is even before the discovery of the tubercle bacillus.²

Iskrant and Rogot³ analyzing trends in tuberculosis mortality in continental United States, show that mortality is now the lowest in history, and that the greatest improvements have occurred in recent years. Nevertheless, tuberculosis ranked seventh as cause of death in 1950, and was the leading killer from disease for the 15 to 34 age group. Iskrant and Rogot³ estimated the toll of tuberculosis mortality in terms of potential years of life lost, and estimated that 900,000 potential years were lost in 1950. There are, of course years of life "lost" in morbidity, for the economic and social loss of creative productivity is particularly high in the very age groups where the morbidity is highest.

A joint committee of the National Tuberculosis Association and the Division of Chronic Disease and Tuberculosis, of the Public Health Service, has made estimates on the number of active and inactive cases of tuberculosis in the nation.⁴ They place the number of active cases at 400,000, with 150,000 of that number still undiscovered. As for inactive cases, they estimate that there are 800,000 such in the country, 550,000 still undiscovered. Even these estimates refer only to individuals with demonstrable x-ray shadows, and do not include the far larger group who still have clear x-ray films but who already carry the tubercle bacilli some of whom are destined to develop gross lesions.

Provisional reports on tuberculosis morbidity and mortality for 1952,⁵ indicate that the trends of the past several years were continued in 1952, that is, ". . . substantial decline in tuberculosis mortality but a comparatively small decline in the number of newly reported cases."

Since the morbidity rate and prevalence of infection have not paralleled the decrease in mortality rate, it appears² unlikely that the present rate of decline in mortality can continue undiminished. In any event, it is clear that tuberculosis remains a major killer, a major source of incapacity and social loss, and a leading public health problem.

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Purpose of Paper

The present purpose is to examine the epidemiological rationale for emphasis of tuberculin testing in tuberculosis control.

The "Clinical" vs the "Epidemiological" approach

Instead of confining ourselves to the clinical concern with the host-parasitic reaction—that is, with those reactions sufficiently marked to be regarded as illness, and centered in that phase of the relationships occurring from the onset of symptoms, to recovery or death—we prefer to consider the subject epidemiologically, with concern for the whole host-parasite relationship, from the time the microparasites enter the body, until they are eliminated. Thus we are concerned with the conditions under which transmission of infection takes place, the subsequent time lapse before symptoms, the occurrence of reactions below the threshold of clinical recognition, and the duration of the infectious state.

Recognized characteristics of the host-parasite relationship

Tuberculosis is a *continuum*. It is a continuous process that progresses by infinitesimal degrees, from the moment that the host and parasite meet, through definite ensuing stages to recovery, chronicity, or death. The population of infected individuals may be visualized as occupants of this continuum, stationed in varying numbers at the various stages along its length. An understanding of the disease depends upon the establishment of clear concepts of the full continuum—of a working insight of the disease through its entire span.

Experimental work with animals^{6, 7, 8, 9} has shown that tuberculous begins within one hour after the organisms are introduced directly into the blood stream. The incoming organisms are phagocytosed by neutrophils and focalized at many points in the body. The neutrophils are poisoned in the process, and lose their ability to change shape, so that they cannot elongate for capillary passage, but remain at the capillary entrance and die. Numbers of monocytes arrive, ingest the fragments of the dead neutrophils, then remain as part of the formation of the tubercle. This focalization with tubercle formation occurs simultaneously in many parts of the body, such as brain, spleen, liver, genitourinary tract, and the bones and joints. The lungs, because of their volume and expansive capillary structure, get more foci, and thus more potential clinical tuberculosis, than elsewhere—but any of these foci, anywhere in the body, may be the starting point—or points—of destructive disease. Thus, as Myers says,⁹ ". . . tuberculosis begins within an hour after the tubercle bacilli invade the body. Future happenings depend upon how much it evolves and at what sites. It continues to be tuberculosis at every step as long as tubercle bacilli are alive in the body."

This long range view leads to immediate consideration of the prevalence of the disease—the *true prevalence*, and the *known prevalence*.

The *true prevalence* at any one time would be the total number of cases at a given time, for as Anderson, Sauer, and Robertson say,¹⁰ ". . . it is these cases which, in the aggregate, represent the actual and potential reservoir of infection and which require case-finding facilities, public

health supervision, and medical care in order to prevent or alleviate disability and economic loss from the disease."

Known prevalence in this country has been arrived at through mortality and morbidity figures, both of which have inherent weaknesses in elucidating present and future tuberculosis problems.

Mortality has never been a reliable criterion of the tuberculosis situation. It is even less reliable now that current treatment methods are extending the lives of tuberculous persons.¹¹ Moreover, in some states more than 25 per cent of all deaths from tuberculosis are first known to health departments through the death certificate.¹² In addition, it must be recognized that persons with contagious tuberculosis may die from other conditions without the tuberculosis having been recognized. Dubos and Dubos¹ report that ". . . in a large series of autopsies carried out in New York on persons dying suddenly of causes other than tuberculosis, it was found that almost 5 per cent had lesions (including cavities) showing active and often advanced tuberculous disease which had remained unsuspected."

Morbidity in the past has largely been data on cases newly reported during a given year. Presently, however, there is a concern with *known prevalence*, i. e., "all cases which are considered by the health department at the date of tabulation to be significant for supervision, even though these cases may have been first reported as new cases many years previously. This includes not only active tuberculosis cases but also those with activity undetermined, arrested tuberculosis, or inactive tuberculosis which the health department considers significant for supervision."¹⁰ Even those figures do not indicate *true prevalence*, when by "true prevalence" one means the inclusion of unknown cases in a specified area.

In thinking of cases, unknown or otherwise, one is reminded that a case is a "host reaction of sufficiently characteristic intensity and duration to permit clinical diagnosis."¹³ In tuberculosis this clinical phase makes up only a small part of the spectrum or disease continuum, and since the host-parasite interaction varies greatly in both severity and duration, there are clinical and subclinical cases. These subclinical cases, even though they are below the level of clinical recognition, can fortunately be demonstrated by the resultant change in the response of the skin to antigenic material in the form of the tuberculin test.

The epidemiologic importance of inapparent infections is great in the propagation and survival of the parasite in relation to the human host. The opportunities for communicability increase with the length of time that the parasite and the parasites progeny can multiply and escape from a host. Long infectious periods, especially when they are mild so that the host moves about freely, become potent sources for the spread of infection.

Early diagnosis becomes of paramount importance, important not only because it gives a chance for prevention of breakdown in some persons, and for effective treatment, but also because it affords the best opportunity to prevent the spread of the disease to possible contacts. This is the keystone of tuberculosis control, and even of tuberculosis eradication,

for as was pointed out by Wade Hampton Frost in 1937, ". . . for eventual eradication of tuberculosis, it is not necessary that transmission be *immediately* and completely prevented. It is necessary only that the rate of transmission be held permanently below the level at which a given number of infections spreading (i. e. 'open') cases succeed in establishing an equivalent number (of 'open' cases) to carry on the succession. If, in the successive periods of time, the number of infectious hosts is continuously reduced, the end result of this diminishing ratio, if continued long enough, must be extermination of the tubercle bacillus."¹⁴ The only qualification that Frost placed on his conclusion was to the effect that, "As to the maintenance of this balance, favorable to us, unfavorable to the tubercle bacillus, there are, of course, elements of uncertainty, among them uncertainty as to the stability of our civilization."

The tools for diagnosis are: clinical findings, laboratory findings, the x-ray film, and the tuberculin test. Of these, only the tuberculin is a *specific* test that will indicate the presence of infection, at a time when the lesions are microscopic and asymptomatic.

Tuberculosis developing in the human body can be detected by the tuberculin test within two months after the initial invasion by the tubercle bacilli. At this time the lesions are usually still so small that no other form of examination of the living body could detect their presence.

Teague¹⁵ has said, "It is being recognized and widely accepted that evidence of infection—a positive tuberculin test and especially a recent conversion—becomes more helpful and significant today than in the past. This is true from the viewpoint of the epidemiologist, the diagnostician, and the therapist."

Once a tuberculin reaction is found, it is an epidemiologic agent that can set up a number of salutary reactions. Search can be instituted for the source case of tuberculosis, with the possibility that the search may avert further spread from that source, and may enable the source, himself, to get under treatment. The reactor, himself, may be given the benefits of treatment, if such is indicated, or even in the absence of clinical disease, can be recognized as a member of a high-risk population group, who once identified, can perhaps be spared some avoidable elements of stress and strain, and can be watched for the possibility of shedding organisms.

A third group of beneficiaries, are the people who might otherwise have become infected in due time by the reactor, but who may be spared if the reactor is handled in such a way as to break the chain of transmission.

Life of the Host as a Continuum

We have approached tuberculosis as a continuum. Now let us view the life of the host from that standpoint. The life of the host is also a continuum. It too is a continuous process that progresses by infinitesimal degrees, from its beginning, until death. It too, goes through definite ensuing stages, each of which has its own characteristics of vulnerability, its own special differences in response to the host-parasite relationship,

and therefore, its own special meaning in the overall epidemiology of a chronic disease.

A given population of individuals may be visualized as occupants of this continuum in varying numbers at various age points along its length. An understanding of a disease, depends upon the establishment of clear concepts of the full continuum, and of how that continuum varies from time to time in a given population group, bringing with its variations resultant variations in the epidemiological characteristics of any given disease.

There is need for much work to be done to elucidate the differences of host-response to tuberculous infection at the different age periods—but such material as is available even now, shows some striking features which are basic considerations in any epidemiological approach to tuberculosis control or eradication. Such features include observed differences in host response in early childhood, in adolescence, in the young adult, and in old age.

For example Krause¹⁶ commented that the child was "exceptionally good tolerance of tuberculosis." Yet a child is a veritable "guinea pig" when it comes to being a responsive *in vivo* detector of an open case of tuberculosis in his environment. The intimacy of his life with those with whom he lives, gives ample opportunity for the seeding of the infection, and the limited number of people who touch, or who have touched, upon his life at an early age, narrows the field within which the source of his infection may be located.

The child, and the child's relationship to tuberculosis, change strikingly with the onset of puberty. Whether growth strains are responsible—the onset of the menarche, or other demands on the organism—something happens to the young host, and the host-parasite relationship changes its characteristics, so that there is an abrupt increase in the adult form of tuberculosis in adolescence.

The reasons for these phenomena are shrouded in mysteries, among which is the question of how the host is affected by growth and development. Johnston¹⁷ has just published the record of 20 year nutrition and metabolic study on adolescent girls, most of whom had tuberculosis. It attempts to show that this abrupt increase is related to a failure to meet the nutritional requirements of the adolescent growth period, and that a favorable course of the disease process, once it has developed, may be conditioned to a large extent by the degree to which we succeed in promoting a normal state, and replenishing previously acquired defects. This study was begun as an attempt to determine the incidence of endogenous re-infection in reactors and exposure cases removed from contact. It soon produced evidence that such reinfections were occurring in significant frequency in girls at the period of adolescence.

Rich¹⁸ speaks of the relationship of tuberculosis to adolescence as follows: "The sharp rise in mortality that follows the childhood period of relative safety is associated with the following circumstances: (1) a progressive increase in the incidence of infection; (2) apparently as specific adverse effect of the state of pubescence on resistance; and (3) the be-

ginning of exposure to the stresses and strains associated with a struggle for existence and with childbearing. That other less evident factors may be operative cannot be denied. The most earnest study should be devoted to an elucidation of the factors which influence the development of progressive tuberculosis at this time of life, for the precise reasons that the disastrous effects observed during this period are still for the most part obscure, and the problem is one not only of extraordinary theoretical interest, but of the utmost importance from the standpoint of human welfare."

There is little need to mention here the significance that clinical tuberculosis assumes from adolescence on through 45 years of age, for these are the years that make up the bulk of mortality and morbidity data on which most of the tuberculosis work in this country has been focused.

There is still one more age period which is emerging with increasing epidemiological importance. Myers¹⁹ has shown that tuberculosis among the aged constitutes a prime problem in tuberculosis control because of its prevalence and contagiousness, the incidence of contagious tuberculosis in persons over 50 being higher than in any other period of life. In the United States the highest tuberculosis mortality rates occur among persons 70 and over, and as for morbidity, there is not only the apparent increase due to cases uncovered by more refined diagnostic methods, but an actual increase due to the greater number of infected individuals who now live to be old.

Considering these host-differences which characterize the different age periods, it becomes epidemiologically interesting to notice the population changes which are occurring in contemporary United States.

The United States is becoming a nation of old people, but even as the aged are increasing in number, we are maintaining our youth. During the last decade, while the population over 65 years of age increased 37 per cent, the population under 5 grew 55 per cent.²⁰ These children now are swelling the pre-adolescent group, and in a few years will enlarge the adolescent section of the population.

The implications of these population changes are vast, for these are basic changes in the elementary epidemiological characteristics, those characteristics of time, place and person, which are the start of any analysis of mass disease in man.

Leavell says, "We still need to remind ourselves constantly that the increase of man's life span by 18 years in half a century has more profound medical, economic, and social implications than such developments as atomic energy, air transportation, and modern communication. Increased life expectancy at birth is giving this country a population with an increasing proportion of aged persons and is causing us to retool from programs for controlling communicable disease to plans for dealing with degenerative disease and long-term illness."

The already existent increase in the older age group, and the existent and predictable increases in the adolescent group, are signals for prevention, for they are recognized high-risk groups, and the demonstration of

abnormally high risk attached to a particular age group is a direct indication for preventive action.

Since the opportunity for scatter and chance transmission of the tubercle bacilli are increased in proportion to the length of time the organisms can continue to multiply and emerge from a host—particularly an apparently normal and ambulatory host—we may assume that success in preventing infection of a population will depend largely on the extent to which tuberculosis is diagnosed at an early stage.

To this end there are case-finding programs, using x-ray film, and/or tuberculin testing. X-ray has been widely used in the recent urban case-finding programs aimed at population groups 15 years and over. Such programs have been rewarded by the uncovering of previously unknown cases of tuberculosis, and through them, the location of some of their contacts, and even some of their sources.

We will not go into any detailed consideration of the fact that many of these programs largely miss two of the high-risk age groups, the *threatened adolescents*, and the *threatening oldsters*.

The adolescents are missed because the programs are set to start at 15 years of age. The older group is sought, and where it *does* turn up, a high prevalence of clinical tuberculosis is found. Christie²² reporting on a mass-chest x-ray survey in Washington, D. C., where only 41 per cent of the estimated population was examined, noted that one-fourth of those having tuberculosis were age 55 and over, although that age group made up only 10 per cent of the population examined.

Considering the place of the tuberculin test and x-ray as screening modalities in tuberculosis control, it is clear that x-ray is not a productive finder of *early cases*. Pulmonary lesion demonstration by x-ray is unsatisfactory in many respects. If shadows are seen, they still are not pathognomonic. On the other hand, lesion may be entirely missed, either because they are not large enough to be visible, or are not dense enough to be radio opaque, or because of the fact that 25 per cent of the lungs are not visible in the usual x-ray film, or the lesions may be extra-thoracic. (10-15 per cent of tuberculosis in the human body develops extra-thoracically.⁸

The autopsy is useful in recognizing tuberculosis in the dead. The x-ray has its place in the recognition of the disease, when the disease is advanced to the point of actual illness—symptomatic or asymptomatic—but for *early recognition*, the *sine qua non* is the tuberculin test.

The tuberculin test has a remarkable high reliability. Its rare unreliability is limited to the form of negatives shown in terminal anergy that state of negative tuberculin when death is near, in a fatal case, and an occasional loss of positive reaction at the time of an intercurrent disease. Apart from these situations, the tuberculin test is one of the most reliable tools available to an epidemiologist.

Clinical tuberculosis develops only in the presence of the tubercle bacillus. The tuberculin test permits the infected individual to be identified within eight weeks after the invasion has occurred.

The conversion of reactors from negative to positive—the annual attack

rate—is now somewhat less than 1 per cent per year in most parts of the United States.^{8, 15} In some places where control programs have reached high levels of effectiveness, the proportion of reactors has become as low as 5-8 per cent even among senior students in high school.⁸ In crowded areas with a high proportion of uncontrolled open cases the per cent of reactors runs higher.

The conversion of a tuberculin reaction from negative to positive establishes at once: (1) the reactor is at least a potential case of clinical tuberculosis, and (2) there has been a source of infection.²³ Each of these facts warrants the attention of the epidemiologist.

The source of the infection must be sought. In general the younger the reactor, the more meaningful this phase of the epidemiological approach becomes, owing to the fact that the reactor's youth limits the number of people with whom he may have had contact. Likewise it assures some recency of the contact. In children under 12, emphasis needs to be directed to finding the person who is the source of his infection,²⁴ rather than in x-raying the child reactor.

As for the fact that the reactor himself is a potential case of clinical tuberculosis, there is a persistent myth that only 1 or 2 per cent of infected persons develop clinical tuberculosis. Longitudinal studies do not support this idea. Rathbun's experience²⁵ indicated that the small per cent of girls and boys having first-infection type of tuberculosis furnished at least 75 per cent of the adolescents developing the reinfection type of tuberculosis, which is often fatal.

Bogen²⁶ in his careful analysis of the subject, concluded that ". . . about half of all infected individuals develop clinical tuberculosis, and from 10-20 per cent of them eventually die of the disease. The high risk of disease and death due to infection by the tubercle bacillus justifies increased effort for its prevention."

At one time in the United States, it was thought that tuberculin testing would be useful only in children, but the present low rate of reactors, makes the tuberculin test increasingly important. Many persons are now getting their first tuberculosis infection as adults. At any age, any individual—even an elderly person—who has been a non-reactor to tuberculin, but converts, has been in all likelihood in recent close contact with an open case of tuberculosis.

Anyone, at any age, with a positive tuberculin reaction, should be examined periodically for clinically tuberculosis, for that reactor has tuberculosis just as truly as the person with "clinical" tuberculosis. The difference is one of degree.

Myers has said, "Periodic x-ray film inspection of chests of tuberculin reactors locates chronic reinfection type of pulmonary lesions on an average of two and one-half years before they cause symptoms and usually before they liberate tubercle bacilli. Lesions found in this stage of evolution can usually be successfully treated in much less time than those which have become more advanced and are contagious."²⁷ The epidemiological importance of this must not be missed in relation to that high risk-group,

the late adolescent. Tuberculosis is still the leading cause of death among the group 17 to 37. Death, in general, is preceded by symptomatic disease. If the symptomatic disease was also preceded by a period when the patient could have been identified by tuberculin testing, and his early lesion recognized roentgenologically, then tuberculin testing among these adolescents becomes highly important. The adolescent who at 17 makes up part of the tuberculosis death toll, is an adolescent who two or two and a half years earlier was in the age group which would not have been included in a mass x-ray program. The adolescent group would not ordinarily comprise a rich source of case finding by x-ray, but the fact that they are a *known group of high risk*, and comprise *the same* population group who, within a matter of months, will begin to make up tuberculosis morbidity and mortality, points to the need for childhood and adolescent tuberculin testing with x-rays of those reactors twelve and over—and always a diligent search for source of infection.

Primary infections are the starting point of all tuberculous lesions. Just as pus was once thought "laudable," so primary tuberculosis was until recently regarded as harmless or even beneficial, on the basis of an assumed immunity production. Primary infections are now recognized as the potential hazards they really are. Close and continued observation of reactors is sound epidemiology.

Gedde-Dahl²⁸ has said "It is valuable to find a case by any method. For the person concerned, however, it is of highest importance to have his infection demonstrated at the earliest possible date, and this can be done only by repeated testing of tuberculin-negative individuals."

The appropriateness of control measures vary with the characteristics of the problem, which in turn varies with time, place and person. Thus the appropriateness and efficacy of control measures for a given disease vary from time to time, from place to place, and with the differences that occur in the population groups involved.

The effectiveness of a public health program, largely depends on the nicety with which these determining factors are considered, and with which the modalities of control programs are selected and flexibly adapted to meet the specific requirements of the specific problems.

Applying these principles to the epidemiologic control of tuberculosis, one sees that there is not just one control measure useful in all times, in all places or with all population groups. The choice of control tools requires judgment. There are situations where mass x-ray is an exceedingly rewarding modality, for example as a screening mechanism in large cities. Then, there are other situations where the rate of infection is lower, where tuberculin testing with observation of reactors, and search for source cases, are so effective that they not only bring about "control" but approach true "eradication" not unlike the epidemiologic triumph in the eradication of tuberculosis in cattle.

There is usefulness to the *longitudinal approach* which tuberculin testing makes possible, and there is usefulness in the *cross-sectional approach* of mass x-ray examinations.

The recent mass x-ray surveys in cities of over 100,000 have demonstrated the efficacy of such surveys as a case finding technique, and as stimulators of community interest and action.

Examples of the impressive results attained with tuberculosis control programs built on the basis of tuberculin testing in this country are best exemplified by the eradication programs in Minnesota, where the tuberculosis mortality rate was 107 per 100,000 in 1916, but 6.8 in 1952—one of the lowest in the world.¹ In Grand Rapids, Michigan, the tuberculin test has been used extensively for more than 20 years. At first it was used only for children, but later for persons of all ages. In time Grand Rapids achieved the lowest tuberculosis of any city of its size in the United States.

In Norway, Dr. Tobias Gedde-Dahl²⁸ conducted a program of "tuberculosis matriculation," i. e., the continuous tuberculin testing of the whole population of a west coast region which was divided at the start into a positive and a negative group, with the negative persons being retested at recurrent intervals. In this region where there was a low rate of infection, tuberculin was found more effective than mass x-ray of chests in locating new cases, and so x-ray was reserved for the reactors. It was concluded that the less frequent the occurrence of tuberculosis, the more selective the control method must be, and that the experience demonstrated tuberculosis to be ". . . an infectious disease which has great possibilities of being fought by purely epidemiological means, which permit early detection and treatment of primary infections and their infectious sources."

An increasing number of workers are recognizing that it is not a matter of either/or in regard to these control modalities, but is rather a matter of *when, how, where, and with whom* can the methods be most useful, and under what circumstances can they be judiciously combined, as for instance in the Central Cooperative Clinic Study²⁹ where ". . . as a short cut to the more elaborate longitudinal study, initial screening by mass x-ray survey provides a starting point from which a longitudinal study of a more restricted population may proceed."

Just as has been seen in the epidemiology of typhoid, diphtheria and syphilis, in tuberculosis, as the infection rate lowers in a region, there is an increasing importance in the epidemiological approach as compared with other mass examination methods, and there is more interest in the epidemiological characteristics of the individual case.

SUMMARY

1. Tuberculosis remains a problem throughout the world, and is by no means conquered in the United States, although mortality and morbidity in this country have reached levels where refined epidemiologic methods become increasingly useful, and promise not only "control" but "eradication."
2. The epidemiological approach demands the earliest possible recognition of the "case." In tuberculosis, this is the individual who has his primary infection with the tubercle bacillus. The tuberculin test is the specific tool for this important case finding.

3. The majority of tuberculosis control activities in this country have been focused on the clinical-disease-phase of the long *continuum or spectrum* of tuberculosis. Widening the focus to include earlier pathology offers epidemiological promise.

4. An effective epidemiological approach to tuberculosis necessitates constant scrutiny of changes in population-characteristics, in order that the program may be best adapted to the prevailing population groups.

5. The majority of tuberculosis control activities in this country have been focused on the 15-45 age group, where deaths have been highest. Widening of the focus to include younger children and the aged, may close gaps in control—and in our knowledge of the nature of the disease.

RESUMEN

1. La tuberculosis sigue siendo un problema en todo el Mundo y de ninguna manera se ha dominado en los Estados Unidos, aunque la-mortalidad y la morbilidad en este País han llegado a cifras en que-los métodos epidemiológicos más refinados se hacen más útiles, y estos son prometedores no sólo de "control," sino de "erradicación."

2. El ataque del problema con miras epidemiológicas pide el-descubrimiento más temprano posible del "caso."

En tuberculosis, tal es el individuo con infección primaria-del bacilo tuberculoso. El instrumento específico es la reacción tuberculínica para esta búsqueda de casos.

3. La mayoría de las actividades para dominar la tuberculosis en este País, se han encaminado hacia la fase clínica de la enfermedad del *espectro o el largo padecimiento tuberculoso*.

La ampliación del campo enfocado para incluir la patología-más temprana, es una promesa en epidemiología.

4. Un ataque efectivo epidemiológicamente requiere un escrutinio permanente de los cambios en las características de la población a fin de que el plan se adapte mejor a los grupos en que es más prevalente.

5. La mayoría de las actividades para controlar la tuberculosis en este País, se han concentrado en los grupos de edad de 15 a 45 años, en los que las defunciones son más frecuentes. La inclusión de los grupos de niños más pequeños y de los hombres de mayor edad, corregiría las fallas en el control y en el conocimiento de la naturaleza de la enfermedad.

RESUME

1. La tuberculose reste un problème mondial. Elle n'a en aucun cas disparu aux Etats-Unis. Il faut noter toutefois que dans ce pays, la mortalité et la morbidité ont atteint des niveaux si bas qu'ils nécessitent des recherches épidémiologiques de plus en plus délicates. Ainsi on peut envisager non seulement l'arrêt du fléau mais encore son éradication.

2. L'épidémiologie exige le dépistage aussi précoce que possible de chaque cas. En matière de tuberculose, il s'agit de l'individu chez qui se manifeste une primo-infection par le bacille tuberculeux. Le test tuberculinaire est un élément essentiel de cette première constatation.

3. La plus grande part de l'activité de dépistage de la tuberculose aux Etats-Unis a été basée sur la phase clinique de la maladie tuberculeuse proprement dite. En élargissant cette conception, et en faisant pénétrer dans le dépistage le premier stade de la maladie, on obtiendra des réalisations épidémiologiques pleines d'espoir.

4. Pour amener une connaissance épidémiologique efficace de la tuberculose, il est nécessaire d'étudier sans interruption les modifications qui peuvent survenir dans les caractères de la population. C'est ainsi que l'on pourra le mieux adapter le programme aux groupes démographiques essentiels.

5. C'est sur le groupe des individus âgés de 15 à 45 ans où l'index de mortalité est le plus élevé qu'a été dirigé aux Etats-Unis la plus large part de la lutte antituberculeuse. En étendant ces recherches aux enfants plus jeunes et aux gens âgés, on pourra obtenir un contrôle intégral de la tuberculose. Simultanément, nous perfectionnerons nos connaissances sur la nature de la maladie.

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Pleural Biopsy

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Although biopsy of the thickened pleura was practiced from time to time by most surgeons for the diagnosis of pleural disease in cases presenting unusual problems, no studies of technique, or results, were found in the literature. A series of 21 cases presenting various problems of management and diagnosis were examined with the aid of biopsy and provided the material of this report.

Histopathologic examinations were expected to distinguish between nonspecific inflammation, granulomatous inflammation, and neoplastic disease. Both histopathologic and bacteriologic examinations were also expected to contribute to etiologic diagnosis of infections. Although no reports were found of observations of the pleural reaction to infectious diseases in material obtained at biopsy, data from cultures of latent postmortem tuberculous lesions suggested that tubercle bacilli, if present, would be demonstrable. Opie and co-workers¹ reported that latent tuberculous lesions discovered at postmortem yielded tubercle bacilli on guinea pig inoculation in 76 per cent of fibrocaceous lesions and in 50 per cent of fibrocaseous and calcified lesions. Even fibrous scars yielded tubercle bacilli in 24 per cent of the lesions. Sweany and co-workers² showed that micro-organisms were less often found and histopathologic evidence of healing became more evident with increasing age of pulmonary lesions over a period of from one to seven years.

A number of procedures, both old and new, were described for obtaining histologic and bacteriologic data in pleural and pulmonary diseases. Paracentesis and the examination of pleural fluid, when present, was preferred to pleural biopsy but was not always successful in our hands for the demonstration of additional specific data. Pleural fluid obtained at paracentesis was generally found to contain demonstrable tubercle bacilli in about 40 to 50 per cent of cases that were thought to be tuberculous. A recent report³ showed that pleural fluid obtained at paracentesis contained demonstrable carcinoma cells in about 50 per cent of cases of neoplastic disease of the pleura. After the appearance of a productive pleural lesion and absorption of fluid only biopsy was possible.

Pleural biopsy was believed to be the most appropriate method when the sole or principle lesion was found in the pleura. Biopsy of the lymph nodes of the cervical fat pad might be considered a relatively minor procedure as compared with pleural, mediastinal, and pulmonary biopsy, and

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circumstances might arise when disease present primarily or principally in the pleura, mediastinum, or lung might also involve the cervical fat pad lymph nodes. This would be most likely in cases of Boeck's sarcoid, Hodgkin's disease, or carcinoma which tended to metastasize to lymph nodes.⁴ No observations were reported in the literature of cervical fat pad, mediastinal lymph node, or lung biopsy in cases of pleural disease, however, such as the cases selected for the present series.

After this study was undertaken, the removal of active tuberculous foci from the lung and their examination for tubercle bacilli were carried out extensively, especially in patients receiving chemotherapeutic agents and antibiotics. The relationship of the presence of viable and nonviable bacilli to the type of histopathologic change and their relationships to the use of specific therapy proved of special interest in those studies.^{5,6,7} No comparable observations were made, however, in this series of cases.

Method

Pleural biopsy was undertaken in cases of persistent pleural lesions following pleurisy with effusion. Only cases that presented an x-ray density of sufficient size, opacity and location as to be readily approached by the operative technic described below were considered suitable for biopsy. The cases were of at least two months' duration and no longer believed to have free fluid in the pleural cavity. If pulmonary tuberculosis was present, or if tubercle bacilli were demonstrated in pleural fluid, or from other sources, biopsy was not undertaken. The cases fell into two age groups. Fourteen were veterans of World War II from 21 to 40 years of age, of whom eight were Negroes, and seven cases were veterans of World War I, 41 years of age and older, two of whom were Negroes. Serologic and other methods of diagnosis were used freely, and it is believed that all cases with pleural lesions due to primary atypical pneumonia, tularemia, or brucellosis were recognized, and when these conditions proved an adequate explanation for the pleural lesion the cases were not subjected to biopsy.

The operative procedure was as follows:

The patient was prepared as for any operative procedure by withholding food and administering a sedative and a narcotic. The operative site was chosen at the point of greatest pleural reaction, as shown by the roentgenogram, usually; the eighth rib posteriorly. The skin was prepared in the usual manner and novocain, 1 per cent, injected into four intercostal nerves and infiltrated along the site of the skin incision. A six-inch incision was made lateral to the rib and three or four inches of rib was removed subperiosteally. With the spear pointed knife several portions of pleura were excised, since experience has shown that a diagnostic reaction was not present in all specimens. Usually there was no free pleural space. When a free space was present a small catheter attached to suction was placed in the wound until it was made air tight. All bleeding points were controlled and no attempt was made to obliterate the site of rib resection. Penicillin was instilled in the wound, which was then closed

with interrupted or continuous sutures. Those patients with obliteration of the pleura were returned to the medical ward. When pneumothorax was present postoperatively, treatment to obtain prompt expansion of the lung by aspiration or closed thoracotomy was advisable. Wound healing occurred promptly and the sutures were removed after six or seven days.

The biopsied tissue was separated into two equal parts with sterile precautions in the operating room and one half placed in fixative for histopathologic examination, and the other half furnished promptly and with sterile precautions for bacteriologic examination. Tubercle bacilli were also sought in all cases in microscopic preparations stained with Ziehl-Neelsen stain and examined by one of the authors.

The patients were returned to the ward after operation in good condition. Symptoms occurred that could be attributed to the operation in two cases. In one, a sudden attack of pain in the chest at the site of operation accompanied by dyspnea and syncope occurred five days postoperatively. Roentgenogram showed no change in the lungs and the symptoms disappeared after 24 hours. The operative note stated that the parietal pleura was adherent to the visceral pleura, and it seems probable that a fleeting intercostal neuritis or neuralgia caused the symptoms. In a second case, hydropneumothorax with increased fluid was noted after pleural biopsy. The operative note described the collection of air and fluid in the pleural space at operation. The general course in this case, both before and after biopsy, was that of progressive spreading pulmonary infection with little response to therapy.

The removal of a portion of rib caused no apparent discomfort or morbidity. Indeed, the missing bone was partially replaced within two months and in several cases the site of operation on the rib was not discernible by roentgenogram after about four months.

TABLE I: ETIOLOGY OF PLEURISY IN 21 BIOPSIED CASES

ETOLOGY	TOTAL	NUMBER OF CASES			
		AGE 21-50	AGE 51-55	RACE White	RACE Negro
Tuberculosis	17	14	3	8	9
Carcinoma	3	0	3	2	1
N. American Blastomycosis	1	0	1	1	0
TOTAL	21	14	7	11	10

Results

Table I shows the recognized etiology of the 21 cases of pleurisy that had biopsies performed. Seventeen cases were found to have tuberculous pleurisy, three had carcinoma, and one had North American blastomycosis. The predominating histopathologic findings in the 17 cases of pleural tuberculosis, Table II, were fibrosis, epitheloid cells, and giant cells in all cases. Distinct tubercle formation was seen in 12, and caseation was present in 10. For confirmation of the specific etiology of such granu-

TABLE II: HISTOPATHOLOGY AND BACTERIOLOGY OF
GRANULOMATOUS LESIONS OF THE PLEURA

	HISTOPATHOLOGY		Tubercle Bacilli	BACTERIOLOGY	
	Fibrosis	Caseation		Section	Culture
Present 4	12	2	Acid Fast Bacilli Present	3*	6
Present	5	8	Acid Fast Bacilli Absent	14	3
Absent	0	7	Not Examined	0	8
TOTAL	17	17		17	17

*Results of culture in these three cases were: one positive, one negative, one not examined. Tubercle bacilli were demonstrated in a total of eight cases.

lomatous lesions, cultures proved most productive in that acid-fast bacilli were demonstrated in six of nine cases examined. Microscopic examinations of stained sections were less often positive. Tubercle bacilli were seen in sections from three of the 17 cases. In the latter three culture of the biopsied tissue was positive in one, negative in another, and not done in the third. The diagnosis was therefore confirmed in a total of eight cases by the demonstration of tubercle bacilli. In the remaining nine the diagnosis of tuberculous pleurisy was based on the microscopic demonstration of granulomatous tissue reactions.

Three were found to have pleurisy secondary to carcinoma. In two of these the pleural biopsy showed malignant cells. In the third case, secondary to carcinoma, the pleural biopsy showed nonspecific inflammatory reaction, but bronchogenic carcinoma was subsequently recognized as the principal lesion when bronchoscopy was repeated. The non-specific pleural reaction in this case was in turn secondary to pulmonary atelectasis and pneumonia.

In one case a mycotic infection, North American blastomycosis, was recognized by pleural biopsy that showed yeast-like organisms in tissue that was the site of a polymorphonuclear and granulomatous reaction. Blastomyces dermatitidis was recovered in culture from a co-existing skin lesion.

Table I again shows that in the age group 21 to 40, all 14 cases were tuberculous and the histologic pictures suggested active processes. These patients under 40 represented problems in management. Despite completion of treatment by rest in bed from one to nine months after periods from two to 11 months of illness, further therapy was considered because of the persistence of extensive pleural radiographic densities. Treatment was continued until the lesions were fully stabilized and until signs of activity disappeared.

Cases more than 40 years of age presented diagnostic problems. Five of the seven in this group were referred to the hospital for diagnosis. Pleural effusions or fibrous pleuritis secondary to neoplastic disease or secondary to tuberculosis were suspected in all. A specific diagnosis was thought necessary for prognosis and in order to recommend appropriate palliative therapy for neoplastic disease or hospitalization and rest for

six months or more for tuberculosis. At the present time specific chemotherapy would also need to be considered for tuberculous pleuritis. Following biopsy, rational therapy based on the observed etiology was possible in six of the seven cases, the one exception being a case of bronchogenic carcinoma with non-specific pleuritis.

Little correlation was seen between the duration of the granulomatous lesions believed due to tuberculosis and the histopathologic and bacteriologic findings. The relative proportion of fibrosis, endothelial giant cell reaction, development of symmetrical tubercles, or caseation varied considerably but not in any significant manner with the duration of symptoms. Tubercle bacilli were recognized on microscopic examination of sections only in the earlier cases of two, three, and five months' duration respectively, but cultures were positive at all stages of the disease represented in this series; namely, two, three, five, nine, and 11 months after onset respectively. Lesions which attained the greatest thickness and sometimes contained loculated spaces or potential spaces between parietal and visceral pleura were found chiefly in the older lesions. Extreme degrees of fibrosis, such as the clinician visualizes when he speaks of inactive fibrous pleuritis or scar were not seen.

Antibiotic therapy and chemotherapy were usually not available during the period of this study and were not used systematically. In three cases that received some treatment with streptomycin before biopsy, the tissue changes did not differ from those seen in the untreated cases, and in two of these three cases cultures were positive for tubercle bacilli. More extensive examination in cases receiving specific therapy would be necessary to note any consistent effects of such specific therapy on histopathologic or bacteriologic results.

The outcome of the 21 cases in this series corresponded with the normally expected clinical course of the respective diseases. Eleven of the total of 17 of primary tuberculous pleurisy were followed from six to 31 months after onset to a favorable conclusion. Six cases of primary tuberculous pleurisy were not followed to a favorable conclusion. Three of the latter were still under treatment at the end of observation periods varying from 11 to 26 months. Three lapsed from observation while their condition was active after from two and one-half to five months' observation.

The three patients with carcinoma died after from three to 26 months of illness. Postmortem examinations were performed in the two cases with positive biopsies. Adenocarcinoma was found in one and bronchogenic carcinoma of an unusually anaplastic type in the other. The patient with North American blastomycosis died outside the hospital after 32 months of illness. No postmortem was obtained.

Discussion

Biopsies were uniformly productive of data that confirmed or explained diagnostic data. A specific cause of pleurisy was demonstrated by biopsy of the parietal pleura, with microscopic examination, or with microscopic examination and cultures, in 20 of 21 cases.

The results were consistent with the general experience that in young adults, primary pleurisy with typical course is nearly always due to tuberculosis. No advantage was gained from biopsy as compared with the customary presumptive diagnosis and appropriate therapy for tuberculosis, in the cases 21 to 40 years of age.

Other causes for pleuritis were found in patients over 40. Biopsy was valuable in these cases, first as a source of evidence for carcinoma or mycotic disease, and second for confirmation of the diagnosis or tuberculosis.

Pleural biopsy is not advocated for those patients with a marked degree of thickening of the pleura or with contraction of the chest wall in lesions of apparent or probable long duration without pulmonary parenchymal involvement. The entire lesion should be excised in one piece. In this way the indicated therapeutic procedure and the diagnostic procedure are combined. The result of the treatment of these cases will be presented later.

It is of particular interest in connection with the bacteriologic examination of biopsy specimens in this study, as well as in other studies^{6,7,8} that the tubercle bacillus was nearly always the only micro-organism that was isolated. The bacteriologic examination of biopsied material was more successful in this respect than the bacteriologic examination of postmortem specimens in which the presence of other pathogenic bacteria complicated the technical procedures and complicated the interpretation of the results.

Pulmonary tuberculosis following pleural effusion may sometimes be the result of such persistence of active tuberculosis in residual pleural lesions. More extensive observations would be necessary to determine how often persistent active lesions, sterile scars, or complete resolution, respectively, are the end results of primary pleurisy with effusion. Such observations would be of value in developing a rational goal for chemotherapy of primary tuberculous pleurisy with effusion.

No other studies of the histopathology of the infected pleura of man during life were reported to our knowledge. These observations may, therefore, be considered to have some significance in the study of the pathogenesis of pleural tuberculosis despite their restriction to material obtained from 2 to 11 months after onset from cases with persistent lesions. The data show that whenever roentgenological densities sufficient for biopsy persisted for two to 11 months that active pleural tuberculosis was present. This corresponds with the reports of Sweany² who found healing required from one to seven years in lesions studied at post-mortem in patients dying of causes other than tuberculosis.

SUMMARY

In disease of the pleura of unproved etiology, histopathologic and bacteriologic examination of biopsied tissue from the parietal pleura disclosed the presence of tuberculosis, mycosis, and carcinoma. Such specific evidence was most often needed in patients in the cancer age and was particularly valuable in justifying the use or the withholding of prolonged rest in bed and antibiotics, or palliative therapy for malignant disease.

RESUMEN

En casos afecciones de la pleura de etiología no demostrada, el examen histopatológico y el examen bacteriológico de la pieza de biopsia de la pleura parietal, descubrió la presencia de tuberculosis, micosis y carcinoma. Tal evidencia específica fué más a menudo necesaria en enfermos en la edad del cáncer y fué de valor especialmente para justificar o no el reposo prolongado, los antibióticos o bien el tratamiento paliativo de una afección maligna.

RESUME

En présence d'une affection pleurale dont l'étiologie est indéterminée, la biopsie de la plèvre pariétale a pu permettre de révéler, grâce à l'examen histologique et bactériologique, l'existence de tuberculose, de mycose ou de cancer.

De telles constatations sont particulièrement importantes lorsqu'il s'agit d'individus ayant atteint l'âge du cancer car elles permettent de justifier ou au contraire d'éviter un traitement par le repos au lit prolongé et les antibiotiques, ou la thérapeutique dirigée contre une tumeur maligne.

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The Rehabilitation of Tuberculous Patients Following Major Thoracic Surgical Treatment

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The frequency of recovery and the duration of survival of patients with advanced pulmonary tuberculosis are greatly increased by collapse therapy and especially by the use of modern thoracic surgery.¹⁻⁵ Thus, only 6 per cent of 1820 patients with advanced pulmonary tuberculosis who received some form of major surgery died while at the Olive View Sanatorium during the past 30 years, as compared with 11 per cent of the 5950 patients who received minor collapse measures and 25 per cent of the 7266 who did not receive any collapse therapy. Some of these differences, but by no means all, may be ascribed to differences in the selection of the patients, the treatments acting as a screen for those who were judged too ill to receive them. There is abundant clinical and statistical information, however, testifying to the large part played by collapse measures in lowering the toll in patients with advanced tuberculosis. (Table I).

TABLE I
FATE OF PATIENTS WITH ADVANCED TB,
OLIVE VIEW SANATORIUM 1920-1951

	Rest only	Minor coll.	Treatment Major surg.	Total al
Number Patients	7266	5950	1820	15036
Per cent Died at O.V.	25	11	6	17
Per cent Died later	31	23	12	26
Per cent Disch. Inactive	16	29	33	24

The proportion of patients discharged from the institution with their disease apparently arrested or quiescent is much higher among those who received active treatment. (Table I). Similar differences may also be observed in the fatality rates of these groups after discharge from the sanatorium. Even among those whose disease seemed to be under control at the time of discharge, the later death rate has been lower among those who received collapse.

The results in all groups have been greatly improved since the introduction of chemotherapy in 1946. Late results are not yet available for this period, but the intramural death rates and the mortality within five years of admission shows similar benefit from collapse measures and especially from major surgery, as does also the condition on discharge. (Table 2).

Less information is available regarding the extent of the handicaps imposed by thoracoplasty and other major surgical procedures themselves, and the manner in which they interfere with the resumption of social and

TABLE II
PATIENTS WITH ADVANCED TUBERCULOSIS
Results of Treatment 1920-46

	Rest	Minor	Major	Total
Number Patients	5607	4625	1005	10237
Per cent D in O.V.	27	12	9	21
Per cent in 5 yrs.	57	27	12	45
Per cent Disch. Arr.	17	33	45	29
			1946-51	
Number Patients	1659	1325	815	3899
Per cent D in O.V.	18	8	3	9
Per cent D in 5 yrs.	18	15	8	13
Per cent Disch. Arr.	12	17	26	16

economic status following recovery from tuberculosis. With the aid of a research grant from the Los Angeles Tuberculosis and Health Association, a study has been made for this purpose of the 1820 patients who had been treated by major surgery for advanced tuberculosis at Olive View from 1920 to 1951.

Thoracoplasties had been performed at Olive View as early as 1923, but only 40 such operations had been done prior to 1932 by the old Sauerbruch procedure. Since then more than 3800 thoracoplasty operations have been carried out, usually in multiple stages, as recommended by Dr. John Alexander.⁵ Apical pneumolysis as described by Semb was done in many cases, especially between 1936 and 1942, and limited five rib thoracoplasties have been carried out especially in more recent years. More than 100 direct cavity drainage operations, by Monaldi's closed or Eloesser's flap method, about 100 plombage procedures with paraffin, lucite or other materials, more than 200 extrapleural pneumothoraces and more recently several hundred pulmonary resections evidence the changing enthusiasms,⁶ but thoracoplasty has remained throughout the chief surgical measure. (Table III).

TABLE III
COLLAPSE PROCEDURES AT OLIVE VIEW 1920-1951

	Times	Pts.	Died
Pneumothorax	5782	4050	462
Pneumoperitoneum	1524	900	131
Phrenic paralysis	4091	1000	57
Thoracoplasty	3858	1476	88
Extrapleural Px	238	135	8
Monaldi or flap	109	57	8
Plombage	102	48	3
Resection	95	84	6
Decortication	45	20	1

It is too soon to evaluate the end results in the 815 surgical patients who were operated during the past five years, as the majority of them are still recuperating from their disease, and even among those reporting more than a year after their discharge, many have not yet attempted to go back to work. The 1005 patients who were operated at Olive View more than five years ago, however, were particularly studied for the

evaluation of the late results of such surgery. Of this group, 276 are now dead and 64 are still or again under treatment, so there are 665 survivors to be investigated. Of these 665 survivors, 10 have not been heard from since the year after their operation, but the majority continued to answer the routine follow-up letters for up to 10 years after their discharge.

Half of these 665 patients, or 333, also answered a special questionnaire which was sent out to those whose addresses were still accessible, in 1952. Comparison of the age, race, sex, stage and condition on discharge of the patients who answered the questionnaire with that of those who did not indicated that they were generally similar, and therefore probably representative of the entire group. (Table IV).

TABLE IV
RESPONSE TO QUESTIONNAIRE

	YES	NO
Total	333	332
Male	167	163
Female	166	169
Mod. Adv.	45	58
Far Adv.	288	264
Inactive	183	176
Active	150	156

It is the social and economic rehabilitation of these 333 patients which constitutes our chief interest here. Of the 167 men in this series, 132 are now employed full time, while another 17 report only part time employment, only 18 are not now working. Of the 166 women, 51 are working full time and 17 part time, but 85 are acting as housewives, generally for eight hours or more, so only 13 report no employment. Thus only 31, or less than 10 per cent of the 333 surgical survivors are not now able to work, and the great majority are working full time. The majority of these patients, however, had waited for more than a year after leaving the sanatorium before engaging in full time activities, in addition to the six to 12 months postoperative period in the sanatorium. A high proportion of the women resumed housework soon after return from the institution, but the others generally waited more than two years before returning to work. (Table V).

TABLE V
REHABILITATION AFTER SURGERY
Interval between discharge and going to work.

	M.	F.
Under 12 months	62	45
Over 12 months	63	70
Difficulty in finding work due to Tb.	30	17
Employment information		
Kind of work	148	67
Place of work	81	41

Difficulty in obtaining employment attributed directly to surgery was

reported by 47 patients. Many others, moreover, made special mention of the fact that they had kept knowledge of the operation and their previous tuberculosis secret since they felt that it would have been a hindrance to their obtaining a position if it had been known to the employer. It was repeatedly emphasized that it was the knowledge of the procedure and the disease which proved an impediment rather than any physical handicap resulting from the operation itself.

Only about a dozen patients specifically mentioned working part time for a period before undertaking full time activities, but this is known to have been the case in many others, although there was great difficulty in obtaining part time positions. It is for this reason, sometimes specifically stated, that patients undertook home activities or self-managed occupations, so that they could arrange their own hours. The kind of work that they were doing was described by 215, and more than half that number specified the exact place where they were working. Nearly three quarters of these patients were about equally distributed between clerical, selling, and skilled crafts, while only a dozen mentioned unskilled manual labor and even fewer reported farm work. Of those noting the place of employment, more than half were working in a store or manufacturing plant, but 17 were working in their own home, and an equal number in an institution, usually as an employee in a county hospital for tuberculosis. (Table VI).

TABLE VI
OCCUPATIONAL REHABILITATION

TYPE OF WORK		PLACE OF WORK	
Clerical	50	Store	50
Selling	50	Mfg.	33
Craft	48	Home	17
Service	23	Institut.	17
Labor	22	Farm	3
Misc.	22	Misc.	2

More than 80 per cent of them are now working full time, some of them even more than nine hours a day, though they had been generally told not to undertake extra strain. The majority still take more than the traditional eight hours a day in bed. Rest periods during the day generally appear to be impracticable, but a longer period in bed at night was frequently reported. Thus some who work eight hours a day or more claim to spend 12 hours or more in bed every night. (Table VII).

TABLE VII
HOURS WORKED DAILY

	M.	F.
Under 7	17	70
7-8	100	75
9—	37	8
	DAILY HOURS IN BED	
8 or less	57	38
9-11	92	95
12—	13	27

TABLE VIII
MARITAL HISTORY

	M.	F.
Married	110	93
Single	57	73
Children since discharge	43	23
Number of children	74	26

The disease and operation have not prevented nearly two thirds of these patients from being married, often to other patients; at least 66 of them have had children since their operation. (Table VIII). There were no special complaints regarding the care given these patients while in the sanatorium, and 14 men and 21 women volunteered favorable comment regarding the services they had received. The tuberculosis itself had been apparently arrested in practically all of these patients, but 235, or more than two thirds of them, still have some symptoms from residual changes following the disease. Thus 181 have shortness of breath, consistent with the low breath-holding time reported in the majority of them, 102 still have sputum and 79 a bothersome cough. (Table IX).

TABLE IX
REHABILITATION AFTER SURGERY

	M.	F.
Breath-holding time		
Under 30 seconds	61	78
30 seconds or more	90	41
Complaints		
Shortness of breath	84	97
Expectoration	55	47
Cough	49	30
None	52	46

The majority returned to the same kind of work which they had been doing before they became ill, and of the scores who mentioned their working conditions, only one complained of dust or poor ventilation. Of the 49 who specifically reported receiving aid from Vocational Rehabilitation agencies, several complained that they took various tests for vocational guidance or placement, but received no useful aid in fitting themselves for work or finding a job through such agencies. However, many had continued their general education while taking the cure, and some learned specific trades here or after discharge which they are now following, such as laboratory technique, watchmaking, or radio repair.

One of the most effective means of rehabilitation has been through working in the sanatorium itself. More than a thousand patients at Olive View have gone through the convalescent camps and been paid nominal wages as patient helpers for part-time work while recuperating from the disease, including 142 who have had major thoracic surgery. More than 140 expatients have become regular employees of the sanatorium, including 10 who have had major surgery for tuberculosis, although the Civil Service has refused to employ known post surgical cases during recent years. (Table X).

TABLE X
REHABILITATION AFTER SURGERY

	All Patients	Major Surg.
Number discharged living	15036	1706
Number Convalescent Camp	1142	142
Number Civil Service Emp.	141	10

Extensive programs have been attempted, both in this country and abroad, to assist in the rehabilitation of the tuberculous. Papworth, Preston Hall, the Remploy workshops and the Disabled Persons Act in England, and numerous other projects in other countries have done much to ameliorate the social and economic woes of patients whose disease persists despite rest and collapse measures. Modern surgery and chemotherapy, however, make possible lasting sputum conversion in an ever increasing proportion of previous treatment failures. Nothing is so important for the full rehabilitation of the victim of tuberculosis than the assurance that he is no longer shedding the dangerous germs of the disease.

SUMMARY

The 1820 patients with advanced pulmonary tuberculosis treated by major thoracic surgery at Olive View during the past 30 years have had a much lower death rate, both within the sanatorium and after discharge, and a much higher proportion of discharges with the disease inactive, than those treated by minor collapse measures only or given not even these. The 815 surgical patients operated since the introduction of chemotherapy have had a lower death rate, than those of earlier years, and also did much better than those given only pneumotherapy or rest. The 333 operated on more than five years ago who answered a special questionnaire have been, in general, rehabilitated satisfactorily, chiefly by their own efforts. Most of them are now working full time and are married, and many have had children since leaving Olive View. Shortness of breath on exertion and other symptoms from residual bronchiectasis are frequent, but do not seem to be disabling.

RESUMEN

En 1.820 enfermos con tuberculosis pulmonar avanzada, tratados en Olive View durante los pasados 30 años, hemos tenido mucho más baja-mortalidad tanto dentro del sanatorio como después de la salida y también, una más elevada proporción de altas con la enfermedad inactiva-que en aquéllos tratados con procedimientos menores de colapso y enlos que ni aún estos se dieron.

*Following receipt of this study, and resolutions urging change of policy from the Los Angeles Tuberculosis and Health Association, the Los Angeles County Civil Service Commission, on August 6, 1953, adopted the following rule:

"A thoracoplasty or removal of malignancy shall not be deemed disqualifying after five consecutive years of annual physical examinations and there has been no re-currence of tuberculosis or malignancy during said period and the applicant meets all of the other requirements of this rule."

Los 815 enfermos quirúrgicos operados desde la introducción de la quimioterapia tuvieron una mortalidad menor que los años anteriores y también les fué mejor que aquéllos que se trajeron sólo con neumotórax o reposo. Los 333 operados hace más de cinco años que contestaron un cuestionario especial, en general se han rehabilitado satisfactoriamente, principalmente por sus propios esfuerzos.

La mayoría de ellos, están trabajando tiempo completo y se han casado y muchos han tenido hijos desde que abandonaron Olive View. La-disnea de esfuerzo y otros síntomas de bronquiectasia residual son frecuentes, pero no parecen ser incapacitantes.

RESUME

Les auteurs établissent une statistique sur 1.820 malades atteints de tuberculose pulmonaire grave et traités par des opérations de chirurgie thoracique importante à Olive View au cours de ces dernières trente années. Ces malades ont présentés un taux de mortalité beaucoup plus faible, évalué en tenant compte des décès survenus au cours du séjour sanatorial et après leur départ, et une beaucoup plus grande proportion de départs avec stabilisation que les malades qui n'ont été traités que par une collapsothérapie médicale ou même sans celle-ci. Les 815 malades qui ont été opérés depuis l'introduction de la chimiothérapie ont présenté un taux de mortalité plus bas que ceux des années antérieures, et eurent des résultats supérieurs à ceux des malades qui ne furent traités que par le pneumothorax ou le repos. Les 333 opérés depuis plus de cinq ans qui répondirent à un questionnaire spécial qui leur avait été adressé, ont généralement été réadaptés de façon satisfaisante principalement grâce à leur propre effort. La plupart d'entre eux travaillent maintenant à temps plein et sont mariés et beaucoup ont eu des enfants depuis leur départ d'Olive View. Une diminution de la capacité respiratoire à l'exercice et d'autres symptômes dûs à la dilatation des bronches résiduelle, se sont montrés fréquents, mais ne semblent pas gêner considérablement l'activité.

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Antidyspnoeic Action of Para-Aminobenzoic Acid

Modifications of the Functional Respiratory Indexes in the Patients Treated*

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Benda and Poirot,¹ in 1945, in order to avoid the secondary reactions provoked by intravenous injections of procaine, which was recommended for the treatment of dyspnoea by Dos Ghali, Bourdin and Guiot,² proposed using p-aminobenzoic acid (PAB) in the place of procaine. It is known that the latter, once in contact with the blood plasma transforms itself rapidly into p-aminobenzoic acid and diethylaminoethanol, hydrolysis favoured by the presence of an enzyme, the procainesterase which originates in the liver and thyroid gland. In 1949, one of us in collaboration with Cucchiani Acevedo³ mentioned the results obtained with the intravenous and intramuscular administration of sodium salt of PAB (10 cc. of a 5 per cent solution) in the symptomatic treatment of dyspnoea in patients with pulmonary tuberculosis and bronchial asthma. In order to outline what could be subjective in the clinical improvement often observed and to establish on the other hand the mechanism of the antidyspnoeic action of PAB, we have made the following study.

In a group of chronic bronchopulmonary patients (pulmonary emphysema, pulmonary fibrosis, pulmonary tuberculosis, bronchial asthma) with some apparent dyspnoeic manifestations, we have performed several functional respiratory tests before and after parenteral administration of PAB. Apart from the frequency of pulse and respiration the degree of oxygen saturation of the Hb in arterial blood was established, the inspiratory apnoeic pause and the different spirometric data: vital capacity, complementary and reserve air, minute volume of ventilation and maximum volume of ventilation, ventilation reserve and oxygen consumption were determined. Observing these joint preliminary results and to establish their significance more precisely, we furthermore studied in some patients the blood cytology, the globulo-plasmatic relation and the possible variations of residual air. In table I the sex, age and diagnosis of the 22 cases studied can be found.

Technique

The patients in basal conditions and after a resting period of no less than 40 minutes and sometimes more than one hour were submitted successively to the following tests:

- 1) pulse and respiratory frequency, 2) spirometric exploration, 3) after

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TABLE I

Observation	Sex	Age in Years	Diagnosis
1	M	43	Pulmonary emphysema. Pulmonary tuberculosis
2	M	51	Bilateral pulmonary tuberculosis. Spasmodic bronchitis
3	F	26	Bilateral pulmonary tuberculosis
4	M	44	Bronchial asthma
5	M	29	Giant bilateral ampoullous pulmonary emphysema
6	F	28	Bilateral pulmonary tuberculosis. Left pachypleuritis
7	F	29	Bronchial asthma. Diffuse pulmonary fibrosis
8	M	60	Bronchial asthma. Diffuse pulmonary fibrosis
9	M	57	Bronchial asthma and pulmonary fibro-emphysema
10	M	50	Pulmonary emphysema
11	M	73	Asthmatiform chronic bronchitis
12	M	32	Left thoracoplasty; right pulmonary fibro-emphysema
13	M	50	Pulmonary tuberculosis. Pulmonary emphysema
14	M	31	Bronchial asthma and pulmonary emphysema
15	M	56	Bronchial asthma and pulmonary emphysema
16	M	33	Bilateral bullous pulmonary emphysema
17	M	50	Pulmonary emphysema and asthmatiform bronchitis
18	M	36	Pulmonary emphysema; right postpneumothoracic pachypleuritis; right apical cavity
19	M	30	Bronchial asthma and pulmonary fibro-emphysema
20	M	40	Diffuse interstitial pulmonary fibrosis
21	M	59	Bronchial asthma; pulmonary tuberculosis and fibro-emphysema
22	F	54	Bilateral pulmonary tuberculosis

a supine resting period samples of arterial blood were taken (oxymetry) and venous blood (hematocrit and hemogram), 4) intravenous injection of 10 cc. of sodium PAB at 5 per cent solution, 5) 15 minutes after the administration of the drug, the patient maintaining his supine position the second blood extractions were performed, 6) pulse and respiration and apnoeic pause measured, 7) the functional respiratory test repeated. In one case (observation 21) the arterial oxymetry was established at three different moments: before the PAB injection and 15 and 60 minutes after. In two patients (observations 6 and 22) the drug was administered by intramuscular injection during 10 days (two injections of 10 cc. of 5 per cent solution). The arterial blood analysis was made just before the treatment was initiated and twice more during the course of the same with four to five days intervals.

The arterial blood was extracted by puncture of the femoral artery and kept under anaerobic conditions; the arterial saturation of Hb and O₂ blood capacity were measured in the van Slyke apparatus by the manometric method. The functional respiratory examination was made in an apparatus of the Knipping type and for the residual air determinations the method of Christie, modified by Chiodi was used. The globulo-plasmatic relation was determined with hematocrit.

Results

The oxymetry of the arterial blood, determined in 17 patients, shows that the arterial Hb saturation improves in almost all the cases where PAB was used. When the drug was administered intravenously (in 16 cases with 18 double determinations, one immediately before the injec-

tion and the other 15 minutes later) a moderate increase in the saturation was observed in 15 determinations out of 18, three remained unchanged. In one of these last cases (observation 21) the analysis of the arterial O₂ was repeated 60 minutes after the injection and a pronounced elevation of the Hb saturation was obtained: from 82.0 to 92.2 per cent, coinciding with evident clinical improvement. The promedium of the quantity of arterial O₂ in cc. reached an 18.0 in previous per cent analysis and 19.6 in those following PAB administration. The difference of Hb saturation is expressed in numbers such as 85.9 per cent before and 92.6 after the PAB injection respectively (table II).

TABLE II: ARTERIAL OXYMETRY

Determinations before and 15 minutes after the intravenous injection of PAB						
Observation	Date	Capacity cm ³ %	Quantity Before	Quantity After	Saturation Before	Hb% After
1	30-VI-51	21.68	18.09	21.06	83.40	96.80
	5-VII-51	21.74	19.82	21.22	91.10	97.50
2	14-VIII-51	23.37	20.33	22.05	86.90	94.30
	14-VIII-51	20.42	18.13	19.60	88.70	95.90
3	20-X-51	18.68	16.84	17.60	90.10	94.20
4	25-IX-51	20.58	17.39	18.37	84.20	89.20
5	9-X-51	21.17	13.30	19.80	72.20	93.50
6	2-XI-51	17.50	15.35	16.30	87.0	93.10
8	5-IV-52	23.84	21.15	21.89	88.70	91.30
9	8-IV-52	20.83	17.20	19.87	82.50	95.30
11	22-IV-52	20.31	19.10	19.87	95.0	97.0
12	8-V-52	23.76	22.29	22.29	94.0	94.0
13	8-V-52	16.17	11.50	12.72	72.0	79.0
14	15-V-52	23.67	20.75	20.75	88.0	88.0
15	15-V-52	20.26	17.33	19.77	86.60	98.80
16	17-V-52	20.58	17.39	19.36	86.90	96.80
19	24-VI-52	23.93	20.97	21.96	87.60	91.40
21	8-VII-52	22.98	18.86	18.86	82.07	82.07
Averages		21.19	18.09	19.62	85.94	92.67

The increase of the arterial Hb saturation percentage can be noted specially in patients with low Hb saturation so that in the first cases (observations 1 and 2) it was decided to repeat the therapeutic test, but after several days or weeks the results were similar to the initial ones. The greatest improvement was observed in a patient with pulmonary bilateral cystic emphysema (observation 5) where the Hb saturation increased from 72.2 to 93.5 per cent after use of the drug.

In the two cases submitted to repeated intramuscular injection of PAB an increase of the Hb saturation was observed in each analysis with intervals of four to five days (table III). In one of the patients (case 22) the respiratory rate and the pulse decreased, a fact which could not be observed in the other case (6) may be because of a pleural incidence with temperature which she suffered at the time. This same patient was submitted months later to the intravenous therapeutic test; the results have been discussed already (table II).

The action that PAB produces in conditions of arterial oxygen insaturation does not depend on the comportment of asthmatic or related mani-

TABLE III: ARTERIAL OXYMETRY

Determinations before and during the treatment with intramuscular PAB						
Observation	Date	Capacity in cc. %	Quantity in cc. %	Saturation Hb %	Respirations	Pulse
6	29-VIII-50	17.64	11.51	65.00	32	120
	2-IX-50	17.52	12.74	72.80	24	120
	7-IX-50	17.88	14.21	79.70	32	124
22	22-VIII-50	14.70	13.40	91.63	32	86
	26-VIII-50	14.90	13.80	92.61	26	80
	30-VIII-50	15.40	14.90	96.60	22	76

festations. In order to exclude the possibility that the results obtained were due to the increase of circulating hematics in seven cases the blood cell volume before the injection and 15 and 60 minutes after the same was determined with the hematocrit. No significant modifications were observed (table IV), and the same applies to the red blood cell count and

TABLE IV: CELLULAR VOLUME

Percentages obtained with the hematocrit before and after the intravenous injection of PAB			
Observation	Before	After 15 min.	After 60 min.
1	51.5	51.5	52.5
2	51.5	51.3	—
6	48	46	46.5
15	48	49	48.5
17	50	51	51
18	51	49.5	48.5
Normal individual	49	47.2	48
Averages	49.8	49.3	49.1

leukocytes or in the leukocytic hemogram performed in a normal subject under the above mentioned conditions and a patient with respiratory insufficiency.

On account of its greater interest we analyzed first the *oxygen consumption* of the functional respiratory examinations. In 22 determinations from 19 patients (table V) decrease of O_2 consumption was observed 16 times after PAB administration, four times increase and twice no change. The consumption promedium per minute before and after the injection is 301.8 cc. and 241.3 cc. respectively. In the 16 determinations where the oxygen consumption decreases the medium reduction reaches 91.8 cc. (13 times with numbers superior to 40 cc.), on the other hand in the four cases with increase the number were 35 cc. average (in two cases superior to 40 cc.). To judge these results we remembered that the 40 cc. volume is generally accepted as the technical error limit for the Knipping apparatus used for functional exploration. In order to find their statistical significance the technique of X^2 per cent was applied receiving $X=4.3681$ which explains the appearance of 3 results in 100.

The respiratory quotient was determined in three patients, but after PAB injection modifications were not observed.

TABLE V: OXYGEN UPTAKE IN CC.

Determinations performed before and 15 minutes after the intravenous injection of PAB

Observation	Date	Oxygen uptake in cc.		
		Before	After	Difference
1	30-VI-51	280	140	-140
	1-VII-51	200	150	- 50
2	14-VII-51	285	240	- 45
	14-VIII-51	290	290	=
3	20-XI-51	200	260	+ 60
4	25-IX-51	260	150	-110
5	9-X-51	280	340	+ 60
6	20-VII-51	250	240	- 10
7	16-X-51	240	250	+ 10
8	5-IV-52	250	240	- 10
9	8-IV-52	270	190	- 80
10	19-IV-52	250	250	=
11	22-IV-52	350	260	- 90
12	29-IV-52	290	120	-170
13	8-V-52	230	240	+ 10
14	13-V-52	790	500	-290
	15-V-52	450	360	- 90
15	15-V-52	275	240	- 35
16	17-V-52	320	200	-120
17	17-VI-52	300	190	-110
20	28-VI-52	310	260	- 50
21	27-VI-52	270	200	- 70
Averages		301.8	241.3	

The *apnoeic pause* increased in 19 cases from 26.2 to 30.2 seconds average.

Several spirometric tests which were performed 21 times in 19 patients showed the following modifications after PAB was injected (table VI) :

TABLE VI: SPIROMETRY

Average of 21 determinations in 19 bronchopulmonary patients before and 15 minutes after the intravenous injection pf PAB

Determinations	Before	After
Inspiratory apnoeic pause	26 sec.	30 sec.
Vital capacity	2046 cc.	2132 cc.
Complementary air	1068 cc.	1060 cc.
	502 cc.	624 cc.
Minute respiratory volume	11.4 l	13.1 l
Maximum respiratory volume	39.5 l	42.3 l
Reserves of ventilation	65.5%	64.4%
Number of respirations	28	24
Pulse frequency	93	89

Vital capacity from 2046 cc. to 2132 cc. promedium (increase 15 times, unaltered once and lower numbers in five cases). The *complementary air* volumes maintained their relation (ten times increase, four times no change and seven times lower); increase of *reserve air* from 502 cc. to 624 cc. (the numbers were superior 15 times and inferior six times); increase of the *respiratory minute volume* from 11.4 liters to 13.1 liters

average (16 times higher, twice lower numbers and thrice the same); the maximum respiratory volume increased from 39.5 liters to 42.3 liters promedium (higher numbers 14 times, equivalent twice and four lower); no significant variations in the ventilation reserve percentage. Observing these last tests it was considered that the increase of the respiratory minute volume was the most outstanding feature.

The respiratory frequency decreased from 28 to 24 per minute in average. Out of 15 cases the number of respirations was lower in 11 and in the four others no change was observed. The influence of PAB on the pulse rate was less noticeable: in 21 determinations three times more rapid, six times without modifications and 12 times slower.

In conclusion it can be pointed out that in the functional respiratory examination the pulmonary ventilation in rest shows that the tidal air increased more relatively than the reduction of the frequency of respiratory movements (more profound respirations) after intravenous administration of PAB at the same time there is a slight increase of the apnoeic pause and the vital capacity.

In three patients the residual air was determined and also its relation to the total pulmonary capacity but there were no significant modifications (table VII). This investigation was realized on account of the im-

TABLE VII: RESIDUAL AIR

Observation	Functional residual air		Residual Air		Relation of the residual air to the total capacity	
	Before	After	Before	After	Before	After
1	3254	3513	2664	2713	66.3%	62.2%
15	3100	3075	2140	2375	37.8%	40.9%
16	4164	4071	2864	2711	44.6%	44.2%
Averages	3504	3553	2556	2599	49.5%	49.1%

provement of the arterial oxygen saturation which could mean a diminution of the residual air volume, since the majority of patients suffered from pulmonary emphysema associated in some cases with other anatomofunctional alterations.

The treatment produced in many cases a rapid subjective improvement of the dyspnoeic state of the patients, more marked in asthmatics and in some cases the existant cyanosis diminished.

Commentaries

The study of the respiratory function in anoxemic patients through bronchopulmonary disturbances shows that the parenteral treatment with PAB acts favourably on the oxygen content of arterial blood increasing the amount of the saturated Hb percentage. This result does not appear to depend on the better pulmonary ventilation, in spite of an increase in

both respiratory volumes (minute volume and maximum volume) considering that at the same time a paradoxical decrease of the oxygen consumption is apparent. If for a moment we disregard this comprobation, although very interesting, it should be added that this oxygen increase of arterial blood does not correspond to an exclusive bronchospasmolytic action, since it has already been observed in patients with and without asthmatic manifestations and the values of residual air remain unchanged. Nor could it be attributed to an increase of the circulating hematics observing the results of the red blood cell count and the cellular volume measured with the hematocrit.

In hypothesis: to understand the mechanism of the action of PAB in the treatment of dyspnoea, the functions of the drug itself should be analyzed and also pharmacological properties of procaine, of which PAB constitutes part of the molecular nucleus. Intravenous procaine acts in many different and complex ways which explains the variety and the ample uses for its therapeutic application. Added to this problem should be remembered a) its amphoteric action on the automatic nervous system with inhibition of the sympathetic or parasympathetic system depending on the organic tonus (Hazard,⁴ Frammel,⁵ etc.); b) its spasmolytic action (bronchial and vascular) to which an antiallergic influence can be added similar to some synthetic antihistamines (Hazard and Corteggiani,⁶ Halpern,⁷ Frommel⁸); c) its stimulating action on the pulmonary ventilation and oxygen consumption (Sosa Gallardo,⁹ Mirto¹⁰); d) its influence on the blood cytology with immediate increase and the transient augmentation of the number of red and white blood cells because of the adrenergic effect accompanied by contraction of the spleen (Warembourg, Fontan and Michel¹⁰). Of these different mechanisms some are in clear discordance with the results referred to above and others fail to explain themselves satisfactorily. Thus it should be searched for the PAB's proper functions and whether they are capable of satisfying this question.

Investigations conducted in the last 10 years have shown the interesting and manifold activity of PAB in biology with its combined vitaminic, bacteriostatic and pharmacodynamic properties which have led to its therapeutic use in a great number of morbid conditions. Regarding its anti-dyspnoeic action and the modification of the functional respiratory indexes, specially the oxygen arterial blood increase with reduction of the oxygen consumption, two different mechanisms can be assumed. One that the PAB favoured catalytically the intraorganic oxidation, the same as the other acids (succinic, fumaric, malic acid, etc.) which improve or facilitate the utilization of oxygen in the tissues in anoxic conditions as was shown *in vitro* by Proger, Asiner and Squires¹¹ and confirmed by Castex and collaborators¹² regarding the clinical applications of succinic acid. This first hypothesis may be criticized because the above mentioned catalytic agents belong to the aliphatic organic acid group whereas para-aminobenzoic acid is a benzene ring compound. The second mechanism concerns itself with the antioxidantizing activity of PAB which was verified experimentally by György and Tomarelli¹³ and which Bergel¹⁴ was study-

ing lately. The antioxgens are capable of delaying or retaining the oxidation of fatty substances by direct action or through the inhibition of the pro-oxygens, figuring in the first place the copper. Undoubtedly, the anti-oxygenic capacity of PAB can be connected with its antithyroid and goitrous action, established by Mackenzie¹⁵ and Astwood.¹⁶ Gordon and co-workers¹⁷ demonstrated in experiments with rats that the addition of PAB to their diet during several weeks reduces the oxygen consumption in 25 to 35 per cent, the same result as has been observed in thiouracil treatment. Basing ourselves on all these facts we believe that the functional respiratory modifications observed in our patients treated with PAB are principally due to the antioxidantizing action of this substance. As a matter of fact, the effect of the compounds which favours or inhibits the oxydation processes is not always constant so that under certain conditions antioxgens can act like pro-oxygens or vice versa.

SUMMARY

In 22 chronic bronchopulmonary patients with respiratory insufficiency and varied degrees of dyspnoea the functional modifications after intravenous or intramuscular para-aminobenzoic acid administration were established. Fifteen minutes after the intravenous injection (10 cc. of sodium salt at 5 per cent) an increase of oxygen in arterial blood and the hemoglobin saturation (from 85.9 to 92.6) could generally be observed, and the oxygen consumption decreased (from 301 cc. to 241 cc. average per minute). The apnoeic inspiratory pause increased (from 26 to 30 seconds), the vital capacity (from 2046 cc. to 2132 cc. average), the reserve air (from 502 to 624 cc.) the respiratory minute volume (from 11.4 to 13.1 liters), the respiratory maximum volume (from 39.5 to 42.3 liters) and the number of respirations diminished (from 28 to 24 per minute). It is being considered that the favourable action of PAB on the anoxic states of bronchopulmonary origin is principally due to its antioxidantizing capacity.

RESUMEN

En 22 enfermos broncopulmonares crónicos con insuficiencia respiratoria y disnea más o menos aparente se estableció las modificaciones funcionales consecutivas a la administración de ácido para-aminobenzoico por vía endovenosa o intramuscular. A los 15 minutos de la inyección endovenosa (10 cm³ de la sal sódica al 5%) se comprobó generalmente aumento de la cantidad de O₂ en la sangre arterial y del porcentaje de saturación de la hemoglobina (de 85.9% a 92.6%), disminución del consumo de oxígeno (de 301 cm³ a 241 cm³ por minuto), aumento del tiempo de apnea inspiratoria (de 26 a 30 segundos), de la capacidad vital (de 2046 cm³ a 2132 cm³), del aire de reserva (de 502 cm³ a 624 cm³), del volumen respiratorio minuto (de 11.4 a 13.1 litros), del volumen respiratorio máximo (de 39.5 a 42.3 litros), y disminución del número de respiraciones (de 28 a 24 por minuto). Se considera que la influencia favorable del ácido para-aminobenzoico en los estados anóxicos de origen broncopulmonar es debida principalmente a su acción antioxidante.

RESUME

Les auteurs ont étudié chez vingt-deux malades atteints d'affections broncho-pulmonaires avec insuffisance respiratoire et dyspnée de degré variable, les modifications fonctionnelles obtenues par l'administration par voie intra-veineuse ou intra musculaire d'acide paraamino-benzoïque. Quinze minutes après l'injection intra-veineuse (10 cc. de sel de sodium à 5%) on observe généralement une augmentation de l'oxygène du sang artériel et de la saturation en hémaglobine qui passe de 85.9 à 92.6; la consommation d'oxygène décroît de 301 cc. à 241 cc. en moyenne par minute. Le temps d'apnée inspiratoire augmente (de 26 à 30 secondes), la capacité vitale passe en moyenne de 2046 à 2132 cc., le volume de l'air expiratoire de 502 à 624 cc. en moyenne; le volume respiratoire maximum passe de 39.5 à 42.3 litres et le nombre des respirations diminue de 28 à 24 par minute.

Les auteurs estiment que l'action favorable de l'acide para-amino-benzoïque sur l'anoxémie d'origine broncho-pulmonaire est due avant tout à sa capacité anti-oxydante.

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Pulmonary Edema, Etiology and Therapy*

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Introduction

Pulmonary edema can be defined as the escape of serous fluid from the pulmonary capillaries into lung tissue, alveoli, bronchioles, and bronchi. Acute pulmonary edema as a complication of thoracic surgery is found with relative infrequency at the present time except in patients undergoing cardiac surgery. Patches of pulmonary edema are probably frequent in persons with atelectasis or pneumonia. Areas of pulmonary edema are found in nearly all necropsies.

Etiology

Edematous lung tissue is voluminous and heavy, and it will pit when pressed. The alveoli and bronchi of the edematous lung contain serous or blood tinged fluid which can be expressed from the cut surface of the lung.

Lymph fluid is formed by fluid transuded from the pulmonary capillary into the wall of the alveolus. Fluid transuded from the pulmonary capillary can be removed by the lymphatic collecting ducts or the fluid can move into the alveoli and bronchioles and then be expectorated. The pulmonary capillaries can reabsorb water and electrolytes but not plasma proteins.

Drinker has pointed out that pulmonary edema develops when lymph fluid forms in the lung faster than it can be removed by the lymphatic system. In the normal individual, the pulmonary capillary blood pressure of 10 millimeters of mercury tends to transude fluid into the relatively loose lung tissue. The osmotic pressure of 25 to 30 millimeters of mercury exerted by the plasma proteins exerts a stronger force to retain fluid in the pulmonary blood vessels. The intra-alveolar air pressure drops to approximately minus 5 millimeters of mercury on quiet respiration and favors the transudation of fluid from the capillaries. (Figure 1).

Many aspects of pulmonary edema have been studied. Drinker has shown that anoxia in the dog will cause an increased lymph flow in the lung. As the fluid in the alveoli and bronchioles is churned to froth, the anoxia is increased and produces a further leak of fluid from the anoxic pulmonary capillary. This mechanism is one of the major factors in producing pulmonary edema.

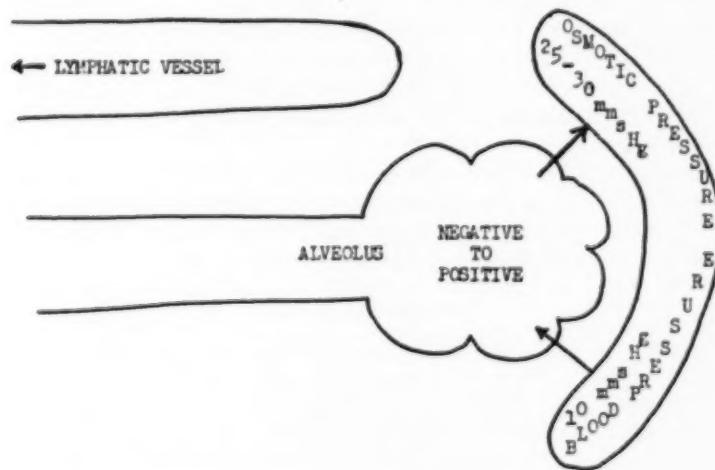
Changes which increase the hydrostatic pressure in the lung capillaries or lower the osmotic pressure of the blood have been studied in various ways. Cournand has demonstrated by cardiac catheter studies that a

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normal person can have a considerable increase in pulmonary blood flow without change in the pulmonary artery pressure. Riley et al. found a decrease in the pulmonary artery pressure when a normal subject exercised. Draper et al. reported in mitral stenosis and mitral regurgitation that the pulmonary artery pressure rose with exercise with no increase in the pulmonary artery blood flow. The resultant increase in pulmonary capillary blood pressure favored the production of pulmonary edema. McMichael reported a 33 per cent increase in the cardiac output of the normal individual when the position was shifted from the erect to the recumbent. If the left ventricle were weak, this increase in cardiac output might well result in increased pulmonary capillary pressure. Liljestrand et al. and Nylin stated that in the normal person work caused no increase in heart size and no decrease in vital capacity, but a shift in position from the erect to the recumbent position caused the heart size to increase and the vital capacity to decrease.

Hemorrhage of 25 per cent of the blood volume in the dog was found by Eaton to double lung lymph flow in 45 minutes. If the hemorrhage were followed by intravenous saline infusion, the lung lymph flow increased markedly. If the hemorrhage were followed by blood or plasma, the lung lymph flow was not elevated. Beattie et al. have found pulmonary edema in the dog given excess blood. Saline infusion into the carotid artery of the normal dog if given in amounts equal to 230 per cent of the blood volume regularly caused pulmonary edema as reported by Luisada. Altschule et al. and Heyer et al. showed that intravenous fluids caused an increase in heart size and a decrease in vital capacity. Stead has pointed out that pulmonary edema can occur with normal or increased body water. He cited



(after Drinker)

FIGURE 1

the instance where a normal individual suddenly developed acute pulmonary edema following a massive myocardial infarction in contrast to the cardiac patient who slowly accumulated excess body water over a period of weeks. In this latter instance, the edema is due to inadequate renal excretion of sodium chloride, probably due to the decreased renal blood flow secondary to the cardiac failure. Water excretion by the kidney is under the control of the anti-diuretic hormone (ADH) from the posterior pituitary. The production of this hormone is influenced by osmoreceptors in the course of the internal carotid artery. Elevated osmotic pressure and emotional, neurogenic, and pharmacologic stimuli can stimulate the production of this hormone. Studies by Squires revealed intracellular fluid upsets in congestive failure. These intracellular fluid changes were characterized by lowered potassium concentration, an increase in the osmolarity of solutes, and overhydration.

In summary, the chief factors concerned in the production of pulmonary edema are:

1. *Increased pulmonary capillary permeability.* This is usually due to anoxia.
2. *Increased hydrostatic pressure in the pulmonary capillaries.* This is found when the right ventricle pumps more blood than the left. Lombardo classified the conditions producing passive pulmonary congestion as follows: I. CONDITIONS PRODUCING MECHANICAL INTERFERENCE WITH LEFT VENTRICULAR FILLING. These include mitral stenosis, tamponade, an intrinsic mass in the left auricle, and an extrinsic mass compressing the left auricle or pulmonary veins. II. CONDITIONS WEAKENING THE LEFT VENTRICLE. These include structural disorders such as infarction and inflammation and functional disorders such as anoxia or ectopic tachycardia. III. CONDITIONS INCREASING THE WORK OF THE LEFT VENTRICLE. These conditions are the disorders increasing the resistance such as hypertension, aortic stenosis, and coarctation and the conditions increasing the inflow load, aortic insufficiency, mitral insufficiency, and disorders associated with a high cardiac output (thyrotoxicosis, etc.).
3. *Decreased osmotic pressure of the blood.* The tendency of the nephritic patient with lowered serum proteins to develop pulmonary edema is well known. Hemodilution from excess intravenous fluids will exert some of its adverse effects by diluting the blood proteins.

Clinical Recognition

The clinical picture of pulmonary edema will vary with the severity of the attack. Small, localized, edematous areas are commonly associated with atelectasis and infection in the lung. These areas will probably not be recognizable as pulmonary edema. Paroxysmal dyspnea may occur in patients with hypertension, coronary disease, or aortic valvular disease. This is acute pulmonary edema in its mildest form. A moderately severe form of pulmonary edema can be recognized as cardiac asthma. In this instance the edema is characterized by asthmatic type rales in the lungs.

Heyer and Plotz have shown that there appears to be an associated bronchospasm with this clinical syndrome. The most severe form of edema is clinically recognized as acute pulmonary edema.

The onset of the edema may be gradual or sudden. (Table 1). The patient may complain of oppression or pain in the chest and will be apprehensive. There will be respiratory distress varying from dyspnea to orthopnea. The patient will cough up frothy and perhaps blood tinged

TABLE I: CLINICAL RECOGNITION OF PULMONARY EDEMA

1. Onset gradual or sudden.
2. Oppression or pain in the chest.
3. Apprehension.
4. Dyspnea or orthopnea.
5. Incessant short cough with copious frothy or blood tinged sputum.
6. Pallor.
7. Perspiration.
8. Rales throughout lungs.
9. Blood pressure and pulse rate elevated in less severe cases.
10. Blood pressure depressed in severe cases.

sputum in large amounts. He will be pale and sweaty. Moist rales will be present throughout the lungs. In the less severe cases the pulse rate and the blood pressure will be increased, but in the severe cases the blood pressure will be decreased. (Figures 2, 3 and 4) demonstrate the characteristic x-ray changes.

Treatment

Acute pulmonary edema is a serious complication with a high mortality rate. Sonne and Hilden in 42 patients with acute pulmonary edema found that in 73 per cent the systolic blood pressure was greater than 190 millimeters of mercury. In this group three of 17 died. In 23 per cent of the cases the blood pressure was under 90 millimeters of mercury systolic. In this group three out of four patients died.

Every effort should be made to prevent pulmonary edema. Table 2.

TABLE II: PREVENTION OF PULMONARY EDEMA
IN THE SURGICAL PATIENT

1. Use special care in patients prone to pulmonary edema.
2. Maintain a clear airway with a minimum of dead space.
3. Administer a high concentration of oxygen with a tidal volume sufficient to remove excess carbon dioxide.
4. Replace blood loss accurately while the blood is being lost.
 - a. Do not undertransfuse patient unless patient has an increased blood volume.
 - b. Do not overtransfuse.
5. Administer intravenous fluids with care. Give NaCl equal to the NaCl lost.
6. Elevate head of patient postoperatively if pulmonary edema is expected.

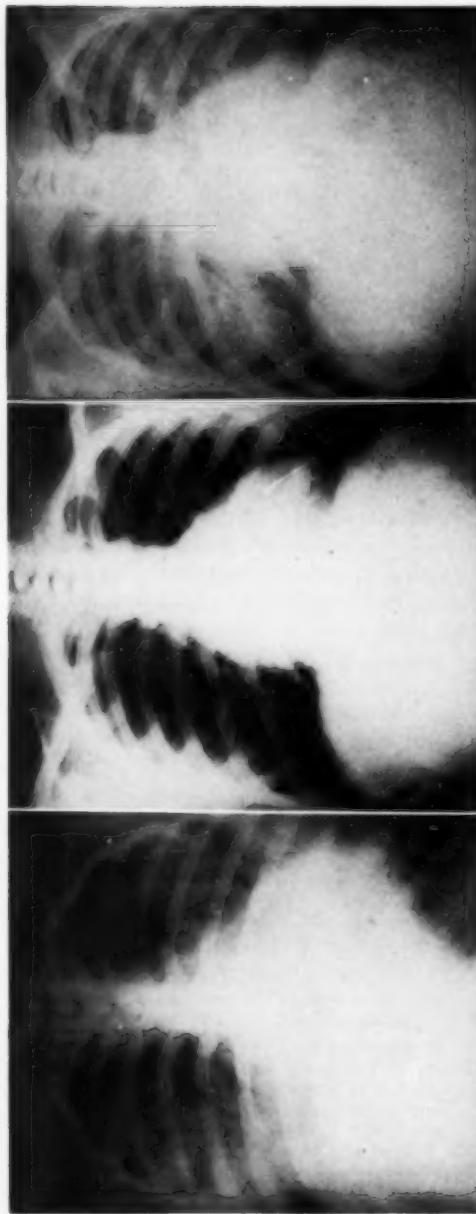


FIGURE 2

Figure 2: Portable x-ray of the chest showing typical acute pulmonary edema.
Figure 3: X-ray of chest from patient with myocarditis and nephritis. No pulmonary edema.
Figure 4: X-ray of chest from same patient as figure 3. Acute pulmonary edema.

FIGURE 3

FIGURE 4

The patient should be examined before surgery to note whether any condition exists which would predispose toward pulmonary edema. The edematous patient should be rid of his edema before surgery. Serum proteins, serum electrolytes, and hematocrit should be normal before surgery. Digitalis should be used when needed.

During the operation and in the convalescent period a clear airway must be maintained. Good intratracheal anesthesia, proper aspiration, and an effective cough are most important. Bronchoscopy and less often tracheotomy may be necessary. The lungs must be kept expanded, and atelectasis and pneumonia prevented. Postoperatively the patient should turn hourly and deep breathing and early mobilization should be encouraged.

A high concentration of oxygen should be used during the operation with sufficient tidal volume to wash out the carbon dioxide. Cardiac arrest should be avoided by avoiding deep anesthesia. Oxygen should be administered postoperatively.

The blood lost during the operation or in the postoperative period should be replaced cubic centimeter for cubic centimeter as it is lost. If an increased blood volume already exists (as in mitral stenosis) or pulmonary edema is anticipated, the patient will benefit from a blood loss up to 500 cubic centimeters. The patient should never receive during an operation more blood than he has lost. A damaged heart tolerates an excess of blood very poorly and serious damage may result from a 500 to 1000 cubic centimeter overtransfusion. If a patient with an increased blood volume is also anemic, it is preferable to give red blood cells without plasma.

Intravenous fluids should be administered with caution during surgery and in the postoperative period. In general, sufficient saline solution should

TABLE III: TREATMENT OF PULMONARY EDEMA

I. Improve Circulation
A. Reduce Venous Return
1. Position
2. Tourniquets
3. Phlebotomy
4. Drugs. Aminophyllin
B. Improve Cardiac Output
1. Digitalis
C. Reduce Peripheral Resistance
1. Aminophyllin
2. Sympatholytic drugs
D. Decrease Reflexes from Engorged Lungs
1. Morphine
II. Improve Lungs
A. Combat Anoxia with Oxygen
B. Combat Hydrostatic Force with Positive Pressure
C. Maintain Clear Airway
Cough, aspiration, tracheotomy, and antifoaming agents.
III. Help Prevent Edema
A. Restrict NaCl Intake
B. Increase NaCl Excretion with Mercurial Diuretics
C. Remove Na with Ion Exchange Resins
D. Aspirate Fluid from Body Cavities
E. Need not Restrict Water Taken by Mouth

be given to replace the saline lost. Usually salt is retained in the body in the first few days postoperatively so that 500 cubic centimeters of isotonic saline per 24 hour period should not be exceeded. The serum electrolytes and urinary chloride can be measured to estimate the need for sodium chloride. If a surgeon restricts saline infusions, he must also be careful not to administer excess glucose solutions intravenously. If a patient on a restricted sodium chloride intake, receives relatively large amounts of parenteral glucose solutions, the total body water may be increased causing a relatively low sodium concentration. This condition (water intoxication, hyponatremia) may have serious results if not recognized and treated. It will usually be necessary to administer concentrated sodium chloride. In the patient prone to develop pulmonary edema this sequence of events will not be beneficial, and it would have been better to re-establish early administration of oral fluids.

If pulmonary edema is feared, it is best to elevate the head of the patient as soon as possible. This tends to lower the venous return to the right heart and to decrease the output of the right ventricle.

If acute pulmonary edema occurs, prompt treatment is essential. Table III summarizes the therapeutic measures indicated:

To improve the circulation. The head of the patient should be elevated to reduce the venous return to the right side of the heart. Tourniquets may be applied intermittently to the extremities to trap several hundred cubic centimeters of blood in the extremities thereby decreasing the effective blood volume and venous return to the right ventricle. The anoxia produced in the extremity will decrease the effective blood volume by causing the capillaries in the extremity to leak serum into the tissue. A phlebotomy of 500 cubic centimeters of blood may be lifesaving. It is thought that aminophyllin has a direct relaxant effect on veins which may aid in diminishing the venous return to the right heart.

If the patient is not digitalized, an intravenous digitalis preparation should be administered to improve the output of the left ventricle. If the output of the left ventricle can be increased in relation to the right ventricle, the lung blood vessels will be partially emptied and the pulmonary vascular congestion will be relieved.

If the peripheral arteriolar resistance could be lessened, the left ventricle could more easily pump blood and relieve the pulmonary hypertension. Sympatholytic drugs have been used for this purpose.

Morphine 10 milligrams should be administered unless there are specific contraindications. Morphine will help allay the anxiety of the patient. Lungs engorged with blood are mechanically inefficient. Churchill and Cope demonstrated that lungs engorged with blood reflexly increased the respiratory rate. The resultant dyspnea in itself has adverse effects because it increases the right ventricular output and lowers the intra-alveolar negative pressure. The latter aids in the transudation of lymph from the engorged capillaries. It is thought that morphine may have a depressant effect upon the reflexly induced dyspnea.

To improve the lungs. Anoxia must be combated strenuously. A snug

fitting face mask should be used with an adequate flow of 100 per cent oxygen. The mask should permit the patient to exhale against an adjustable positive pressure starting at plus 2 to plus 5 centimeters of water. The pressure should be lowered 1 centimeter every one to four hours depending upon the condition of the patient. Positive pressure will combat the increased hydrostatic pressure in the lung capillaries, but excessive positive pressure will interfere with the circulation of blood through the lung and will lower the output of the left ventricle.

A clear airway must be maintained. Cough and aspiration usually suffice. In the unconscious patient with a central nervous system injury tracheotomy is indicated. It is known that the foaming of the edema fluid in the airway aggravates the respiratory distress. Luisada recommended the use of an inhaled anti-foaming agent and found that vaporized ethyl alcohol was beneficial. The usual precautions for explosive anesthetic agents should be used.

To help prevent edema. The measures listed above should be instituted promptly for acute pulmonary edema. The following measures should be employed to prevent recurrence of the pulmonary edema. The daily sodium chloride intake should be restricted to as low as 200 milligrams. The sodium chloride excretion can be increased with mercurial diuretics but care must be taken not to produce hyponatremia. Sodium can be removed from the gastrointestinal tract with ion exchange resins. Fluids should be aspirated from the pleural cavities if it is interfering with respiration. Fluid in the peritoneal cavity may be removed if an excess be present. The intake of salt free fluids by mouth need not be restricted if the daily sodium chloride intake is properly restricted.

SUMMARY

1. Pulmonary edema is the escape of serous fluid from pulmonary capillaries into lung parenchyma. This occurs when lymph forms in the lung faster than it can be removed by the lymphatic system.
2. The chief factors concerned in the production of pulmonary edema are: (1) Increased capillary permeability usually due to anoxia. (2) Increased hydrostatic pressure in pulmonary capillaries when the right side of the heart pumps more blood than the left side. (3) Decreased osmotic pressure of the blood.
3. Small unrecognized patches of pulmonary edema are common. Paroxysmal dyspnea, cardiac asthma and acute pulmonary edema are increasingly severe forms of pulmonary edema. Respiratory distress and copious watery, blood tinged sputum are typical. The blood pressure will be elevated in less severe cases, but decreased in severe cases.
4. Pulmonary edema should be prevented by avoiding anoxia, by preventing pulmonary capillary hypertension, and by maintaining normal osmotic pressures in the blood. To treat acute pulmonary edema the head of the patient should be raised, positive pressure oxygen should be administered, phlebotomy should be done, and digitalis and morphine administered.

RESUMEN

1. El edema pulmonar es el escape de líquido seroso de los capilares pulmonares hacia el parénquima pulmonar. Esto acontece cuando la linfa se forma en el pulmón más de prisa de lo que puede ser canalizada por el sistema linfático.

2. Los principales factores que interviene son:

(1) Aumento de la permeabilidad capilar generalmente debida a la anoxia. (2) Aumento de la presión hidrostática en los capilares pulmonares cuando el lado derecho del corazón bombea más sangre que el izquierdo. (3) Decrecimiento de la presión osmótica en la sangre.

3. Son comunes las áreas de edema pulmonar pequeñas no reconocidas. La disnea paroxística, el asma cardíaca y el edema pulmonar agudo son formas progresivamente severas de edema pulmonar. Los trastornos respiratorios y el esputo copioso acuoso, teñido con sangre, son típicos. La presión arterial estará elevada en los casos menos severos pero decrece en los casos severos.

4. El edema pulmonar debe prevenirse evitando la anoxia, previniendo la hipertensión pulmonar capilar, y manteniendo la tensión osmótica en la sangre.

Para tratar el edema aguda pulmonar la cabeza del enfermo debe elevarse, debe darse oxígeno a presión positiva, hacerse sangría y digital y morfina deben administrarse.

RESUME

1. L'oedème pulmonaire est la pénétration dans le tissu pulmonaire d'un épanchement séreux issu des capillaires du poumon. Cet accident a lieu lorsque la lymphe s'accumule dans le poumon plus vite que le système lymphatique ne permet l'évacuation.

2. Les facteurs essentiels qui peuvent déterminer l'oedème pulmonaire sont 1°) l'augmentation de la perméabilité capillaire généralement secondaire à l'anoxie. 2°) l'augmentation de la pression des capillaires pulmonaires lorsque les cavités droites du cœur pompent plus de sang que les cavités gauches. 3°) la diminution de la pression osmotique du sang.

3. Il existe fréquemment de petites zones d'oedème pulmonaire méconnues. L'oedème pulmonaire se présente sous des aspects plus ou moins sévères de puis la simple dyspnée paroxystique, l'asthme cardiaque jusqu'à l'oedème aigu. La gêne respiratoire considérable, associée à une expectoration abondante, très liquide et teintée de sang, en réalisent les symptômes typiques. La pression sanguine est élevée dans les cas relativement bénins mais elle s'abaisse dans les formes graves.

4. Pour traiter l'oedème aigu du poumon, il y a lieu de surélever la tête du malade, de lui administrer de l'oxygène en pression positive, de faire une saignée, et de prescrire de la digitaline et de la morphine.

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The Treatment of Intrathoracic Hydatid Disease*, **

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Hydatid disease is of comparatively frequent occurrence in Australia, New Zealand, Iceland, Greece and South America. It is endemic in India and, although not of great frequency, it must be considered in the differential diagnosis of any intrathoracic cystic lesion or in any irregular enlargement of the liver.

The proportion of lung to liver hydatids appears to vary in different countries from 60 per cent pulmonary in certain series to as low as 7 per cent in others. Waddle¹ has summarized the material from the Louis Barnett Hydatid Registry of the Royal Australasian College of Surgeons; 478 cases of pulmonary hydatid disease have been reported to the registry from Australia and New Zealand and of these 10 per cent also had liver involvement. He quotes Devé² who showed experimentally that hydatid embryos could reach the mediastinal lymph nodes without going thru the liver. The comparatively low incidence of associated liver and pulmonary lesions makes some such explanation seem plausible. It seems likely that many hydatids do pass thru the liver to reach the lung. As pulmonary hydatids are often asymptomatic until they develop complications or attain considerable size, the number of pulmonary cases detected is proportional to the frequency of chest roentgenological examination. Beckman³ published 13 cases from Sweden, eight of which had pulmonary involvement, and pointed out that five of the eight were discovered in tuberculosis dispensaries where free use is made of roentgenological examination.

Pulmonary hydatids may be divided into two categories, simple and complicated. The simple are those without exogenous daughter cysts or bronchial communication while the complicated ones include those with only a part of the cyst wall and contents is expectorated and a bronchial or pleural communication with or without sepsis.

Pulmonary hydatids may attain large size without any demonstrable bronchial or pleural connection. Such communications occur spontaneously or after some blow or injury to the chest. Although we have had no such experience, apparently the entire cyst may be expectorated and the patient thus cured. This fortunate phenomenon occurred in 36 of Waddle's¹ cases and all but one apparently have no residual symptoms. Frequently only a part of the cyst wall and contents is expectorated and a bronchial fistula persists with superimposed infection. Rupture into the pleural space causes empyema and may produce a severe anaphylactic reaction. As the treatment of uncomplicated hydatid disease is satisfactory, the simple

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cysts should be treated before becoming complicated.

Twenty cases have been treated on our service during the last three years and are the basis of this report.

Diagnosis

An awareness of the possibility of hydatid disease is an important factor in correct diagnosis. In our earlier cases the diagnosis was missed pre-operatively in most as we had not considered carefully enough the possibility of hydatid disease. It must be thought of in any cystic lesion of the lung and the greater the incidence of the disease, of course, the more likely the possibility.

The history is pathognomonic only in those instances where the cyst or its contents has been expectorated, but in other instances suggestive symptoms are forthcoming. In contrast to other cystic lesions, hemoptysis, usually manifest only as streaking of the sputum, has been comparatively frequent even in those cases with no evidence of bronchial communication. This symptom has commonly been held to be indicative of a bronchial communication, but it also probably may be due to a hemorrhagic reaction around the cyst.

In only one of our cases was a history obtained of expectoration of cyst elements. In that one instance the history was unmistakable as the patient stated she frequently coughed up "small bag-like things like the white part of an egg."

Pain has been present frequently. It has not been necessarily in proportion to the pleural reaction noted at operation. Purulent sputum has indicated either an infected cyst or associated bronchiectasis.

The physical examination of the patient has not been helpful in arriving at the proper diagnosis in so far as the specific pulmonary signs are concerned. What has been of help has been the surprisingly good general appearance of most of patients in spite of extensive processes by x-ray inspection. For example, the patient Mrs. R., Case 3, was thought preoperatively to have a large metastatic tumor of the left lower lobe of the lung. Yet she appeared to be in good general condition. This finding should have made us suspect a benign rather than a malignant condition.

Roentgenological study is, of course, the most important method of diagnosis. The various projections usually reveal an apparently cystic mass or masses and frequently some lobulation can be demonstrated. It should also be remembered that hydatids may cause bone erosion by pressure and therefore they may be thought to be malignant.

Other cystic lesions, such as bronchial cysts, pericardial cysts and reduplications of the intestinal tract, are found near the mediastinum in most instances. Hydatids may be present in the same location, but also are frequently more peripheral in the pulmonary parenchyma and may even be wholly in the pleura itself. (Case 2).

Laboratory studies are of considerable value, the most important being the Casoni skin test. The necessary material for testing was not available during the early part of our series and our attempts to make some from the cysts removed at operation were not successful due to contamination.

In those instances where we have done the test preoperatively a positive reaction was obtained in about 70 per cent, and we have not encountered any false positive ones in our short experience.

Eosinophilia may or may not be present. The eosinophils have not been strikingly elevated in any of our cases. In only three of the 20 was the percentage above 12, the two highest being 40 per cent of a 5,800 white blood cell count and the other 28 per cent of a 11,000 count. The level obtained is about the same as that found in other parasitic infestations and as many of our patients have other parasites as well the eosinophilic level has not been of much help.

Aspiration of the cyst by thoracentesis is contraindicated as it may be followed by an anaphylactic reaction, or fluid may leak along the needle tract into the pleural space and disseminate the parasites. Little is to be gained by aspiration. If hydatid elements are found, surgical treatment is indicated. If they are not found, the lesion should be removed in the absence of definite contraindications as simple abnormalities are best corrected while they are simple.

Pneumothorax is rarely a help as it cannot give much information beyond that which is already known, that is, there is a cystic mass in the lung. It does indicate the presence or absence of adhesions, but this is better determined surgically.

Bronchoscopy and bronchography are often used as diagnostic aids, but we have not been impressed with their value as they simply indicate extrinsic pressure on the bronchus. Bronchography is helpful in determining the presence of any associated bronchiectasis or other concomitant lesion. It is usually a good plan to bronchoscope any patient before doing a thoracotomy, but bronchography need not be done routinely.

Treatment

Except for the rare case that expectorates the cyst with its lining complete, practically all cases need surgical treatment. The only method of medical management of which we are aware is the report of Castex and Captehourat.⁴ They propose formation of pleural adhesions, when these are not already present, and then transpulmonary injections of various substances into and surrounding the hydatid. By the hydrostatic effect as well as the irritant action of the material injected coughing is increased and the cyst contents evacuated thru the bronchus! In their report they state they have cured various types of hydatids, both those with previous bronchial communications and those without. No figures are given, however, as to the number of cases treated or those in which the treatment was not effective. They infer that all cases have been successful. In most instances the course of injections extended over many months and it does not appear to be an acceptable method of treatment.

There are two main methods of surgical management. The more frequent type of treatment, according to reports in the literature, is by evacuation of the contents of the cyst and then either draining, marsupializing, or closing tightly the pericyst cavity. The older method was to do this in one stage if pleural adhesions were present or by a two stage method

if adhesions were not found. There is less fear of open pneumothorax or of purulent pleural complications now, so the two stage plan is used infrequently. The more recent reports^{5, 6} of those that advocate evacuation of the hydatid advise open thoracotomy if the pleura is free. The pleural cavity is protected with packs, the contents of the cyst aspirated and then the cyst wall is removed. The outer lining is either closed or drained depending on local conditions. Many believe that formalin should be instilled into the cyst before it is removed to kill any living parasites. It has one disadvantage and that is the rather violent reaction that takes place if any of the formalin gets into the bronchus or pleural cavity. In a recent article Barrett and Thomas⁷ record their experience in some 71 cases. Although they formerly resected most hydatids they now advocate evacuation without aspiration. It is their belief that in most instances even the large cysts do not produce any permanent pulmonary damage and the pulmonary tissue should therefore be preserved.

Marsupialization of the cyst wall to the thoracic wall was often employed a few years ago. Such spaces were a long time in obliterating and this type of operation is not employed now except in some instances with superimposed infection. Even many of the infected cases can be closed with or without drainage⁸ due to antibiotic protection, and thus prolonged morbidity may be eliminated.

In recent years, since pulmonary resection has become commonplace for other intrathoracic lesions, excision has been used more frequently for some types of hydatids. For those of extensive size where practically all of a lobe has been destroyed or when accompanied by pulmonary suppuration, removal of the lobe has been employed with good results. However, one should not sacrifice a whole lobe for a cyst of moderate size that has really but little pulmonary damage. Pulmonary hydatids are often multi-lobar which is another reason for not treating the smaller ones by lobectomy. If the cyst is treated by evacuation the pericystic wall which is laid down by the host remains and this is the "empty sac" that may lead to complications. Barrett and Thomas⁷ state that this pericyst can also be dissected out and removed if indicated. We have not been successful in this maneuver.

The ideal operation would consist of intact removal of the cyst and the surrounding host membrane without sacrifice of normal lung tissue. The operation of segmental resection, as now practiced, nearly achieves this ideal. Newer anatomical studies of the lung have elucidated the subdivision of lobes into lobules or bronchopulmonary segments. Each lobe of the lung is composed of a definite number of these segments (the number depending on the lobe under consideration) each of which has its own bronchus, arterial and venous channels. Those structures are quite constant except for certain minor normal variations. Applying the knowledge of this newer anatomy to actual surgical experience enables the removal of any one or combination of bronchopulmonary segments. The diminution in pulmonary function from loss of any one of these segments is comparatively small and is not to be compared with the diminished pulmonary function following pleural thickening or thoracic wall immobiliza-

tion following a long pulmonary drainage. The operation of segmental pulmonary resection would therefore seem to be adaptable to the treatment of pulmonary hydatid disease, permitting as it does, complete removal of the parasite and its surrounding membranes but with little loss of functioning pulmonary parenchyma. However, it has been possible to utilize segmental resection in only four of our cases.

Brewer, Jones and Dolley⁶ state, "Since the best treatment for echinococcus disease is pulmonary resection, if the condition of the patient permits, pulmonary resection is the procedure of choice." Susman⁸ in a recent article takes exception to this statement. Being an Australian surgeon he no doubt has had a rather large experience with this condition although he does not give his figures in this last report except to state that he had had 12 additional cases since a previous report published in 1948. His earlier paper is not available to us. Susman states that "lobectomy may be necessary for the following conditions:

1. Serious hemorrhage from the cyst space during a conservative operation.
2. Residual bronchiectasis, if symptoms warrant it.
3. Empty sac, if hemorrhage or infection warrants it.
4. When the diagnosis is uncertain.
5. Giant cyst."

In his last article he strongly supports the "conservative" treatment and reports two cases with infection that were treated by evacuation of the cyst but without drainage. No complication ensued.

Our experience with hydatid disease has been limited to 20 cases treated during the past three years. The surgical management of the simple or uncomplicated ones has not presented any major difficulties as all 12 did well following resection. In one, the only one limited to the pleura, simple excision was all that was needed. Seven were treated by lobectomy, two by segmental resection, one by lobectomy and segmental resection and one by bi-lobectomy.

The cases with associated complications such as involvement of the pleura or transdiaphragmatic communications with hepatic hydatids have been difficult problems. Patients with separate hydatids of the lung and liver can be treated as for each infection alone. We have preferred to treat the lung lesion first as the associated liver hydatids were not large in two of our cases, but in one with large liver cysts the abdominal lesion was treated first. In this case two cysts were evacuated abdominally and a third large one in the superior surface of the liver was evacuated transdiaphragmatically at the time of middle lobectomy for the pulmonary hydatid.

The most difficult problems have been the three cases with transdiaphragmatic communications between the liver and lung. In two instances this was on the right, while in one it was on the left. In the latter instances we are not sure whether the infradiaphragmatic hydatid abscess was really hepatic or only subdiaphragmatic as this patient had been operated on twice before for abdominal hydatids and multiple cysts could be palpated throughout the abdomen.

In all three combined cases the liver hydatid was grossly infected at the time of operation and all were drained subcostally as well as thoracically. Long periods of hospitalization were necessary in these three cases and in two of them drains were still in place in the subdiaphragmatic region at the time of discharge.

In only one of our cases were hydatids present in both lungs. A resection of the right middle lobe and superior segment of the right lower lobe was done without incident, but the patient has not returned for treatment of the cyst on the left side.

Case Reports

Case 1: C.M.C.H. 95902, Mrs. V., an 18 year old married woman entered the hospital on August 23, 1949, having been referred by Dr. J. Frimodt-Møller of the Union Mission Tuberculosis Sanatorium, Arogyavaram. Her present illness had started three months previously with a fever of low degree. This continued for five or six weeks. During this time she was given a course of streptomycin (exact amount unknown) although no chest x-ray was taken during this period. After the fever had subsided she had no complaint except for generalized weakness. There was no cough, sputum or hemoptysis. She had noticed a sensation of discomfort over the lower right chest and in the epigastrum. Because of her generalized weakness she presented herself at the Sanatorium for investigation as she had been told that she had pulmonary tuberculosis. Studies there revealed a mass in the superior segment of the right lower lobe, Fig. 1 A and B. The lesion was not entirely spherical, but appeared to be somewhat lobulated and was thought to be cystic. An assistant aspirated the chest in that area and removed two ounces of clear fluid which was studied both chemically and culturally without finding any points of diagnostic significance. Hydatid elements were looked for specifically but not found. Fortunately there was no untoward reaction from the aspiration. She was referred to this hospital for treatment. Physical examination at the time of admission revealed a well developed and nourished young woman in no acute distress. The abnormal physical findings were limited to the right chest where there was evidence of a small pneumothorax and a small amount of fluid in the right pleural cavity. Her temperature, pulse and respirations were within normal limits. Laboratory examination revealed hemoglobin 12.25 gms., white blood count 10,000, the differential showing polymorphonuclears 52 per cent, lymphocytes 26 per cent, monocytes 2 per cent and eosinophils 20 per cent. The Kahn test was negative and her sedimentation rate was 30 mm. the first hour and 70 mm. the second hour. Urine and stool examination showed no abnormalities. A tentative diagnosis of bronchial cyst was made and exploratory thoracotomy was advised.

On August 29, 1949, with the patient in the prone position and under procaine paravertebral block and light ether endotracheal anesthesia, the right thorax was opened thru an intercostal incision. 200 cc. of slightly turbid fluid were found in the pleural space. The superior segment of the right lower lobe was replaced by a cystic mass 7 cm. in diameter. In some parts the cyst was covered by lung and in others a greyish wall was exposed. By blunt dissection an attempt was made to separate the mass from the surrounding lung, but in so doing the cyst was ruptured at the point where it had been aspirated. On opening the cyst a small bronchial fistula was discovered. Believing it to be a bronchial cyst, a segmental resection was done, removing the superior segment of the right lower lobe. This separation was carried out without difficulty. There was little leakage of air or blood from the remaining basal segments. The bronchus was closed with one row of interrupted cotton sutures and reinforced with a flap of pleura. The chest was washed out with saline and drained with one tube posteriorly. She was returned to the ward in good condition, with a blood pressure of 108/70.

Her postoperative course was essentially uneventful. She had a temperature up to 101° F. the first two postoperative days after which it gradually subsided, reaching normal on the sixth postoperative day. She was discharged on the 14th postoperative day. She has remained well since operation and her x-ray film on September 17, 1949, is shown in Fig. 1 C. The pathologic examination of the removed segment revealed two sacs of equal size, one a thick fibrous wall and the other white and gelatinous. Microscopically the structure of the wall was that of an hydatid cyst. There was no evidence of any living parasites.

Case 2: C.M.C.H. 97297, Mr. T., a 35 year old married cooly, was admitted to the hospital on October 25, 1949, because of pain in the left chest of three months' dura-



FIGURE 1A

FIGURE 1B

FIGURE 1C

Figure 1 (A)—Case 1. Preoperative posteroanterior x-ray film of the chest showing a large, somewhat lobulated, mass in the right, lower lung field. (B)—Right lateral x-ray film of the chest showing the mass to lie in the region of the superior segment of the right lower lobe. (C)—Postoperative x-ray film of the chest following removal of the hydatid by segmental resection of the superior segment of the right lower lobe.

tion. The onset of the pain was insidious and really began two years before admission, but had been much worse during the past three months. During the same two year period there had been some cough and expectoration. About every three to four months there were attacks of more severe cough, increased pain and frequently fever of moderate degree. During the past three months sputum had occasionally been brownish in color. Pain in the left shoulder had been gradually increasing making rest at night difficult.

Physical examination revealed a fairly well developed and nourished man in no great distress but complaining rather bitterly of pain beneath the left scapula. There was dullness over the upper part of the left chest posteriorly and quite marked tenderness to pressure. Breath sounds were diminished over the same area. The remainder of his physical examination was within normal limits. His temperature was normal, pulse 62 and blood pressure 90/60. X-ray film of the chest, Fig. 2, revealed



FIGURE 2—Case 2. Preoperative posteroanterior x-ray film of the chest showing a large cystic mass in the left upper chest.

a rounded mass in the left upper lung field posteriorly. The borders were well outlined and there appeared to be no infiltration of the lung. Further x-ray studies of the upper dorsal spine and ribs showed no evidence of erosion although the ribs seemed to be somewhat displaced by the mass. Laboratory examination revealed hemoglobin 16 gms., white blood cell count 4,000 with a differential showing polymorphonuclears 46 per cent, lymphocytes 43 per cent, eosinophils 6 per cent, basophils 1 per cent and monocytes 4 per cent. The sedimentation rate was 2 mm. the first hr. and 6 mm. the second hour. The urine was normal. Examination of the stools showed hookworm ova. A diagnosis of benign tumor of the left upper chest was made and he was advised to have it removed.

Because we considered the possibility of the lesion being a meningocoele, he was operated upon in the lateral position under procaine paravertebral block and light endotracheal ether anesthesia. The usual left parascapular incision was made and the thoracic cage exposed. On doing so a soft, cystic mass was observed presenting between the third and fourth ribs. The fluid was aspirated and some sent for chemical examination, and another specimen to the pathologist. No hydatid elements could be found on microscopic examination. The fluid showed albumin 16 per cent, globulin 17 per cent, sugar 59 mg. per cent, protein 113 mg. per cent and chlorides 590 mg. per cent (subsequent report). A section of the fourth rib was removed and the cyst dissected out. It was found to lie apparently in the pleura as it was not attached at any particular point to the underlying lung. The cyst separated without difficulty from the lung and chest wall although at one place a small rent was made in the pleura. This rent was closed with interrupted sutures. The space was thoroughly washed out with saline and the wound closed in the usual fashion in layers with cotton. He was returned to the ward in good condition.

Postoperatively he had a smooth convalescence, the temperature returning to normal

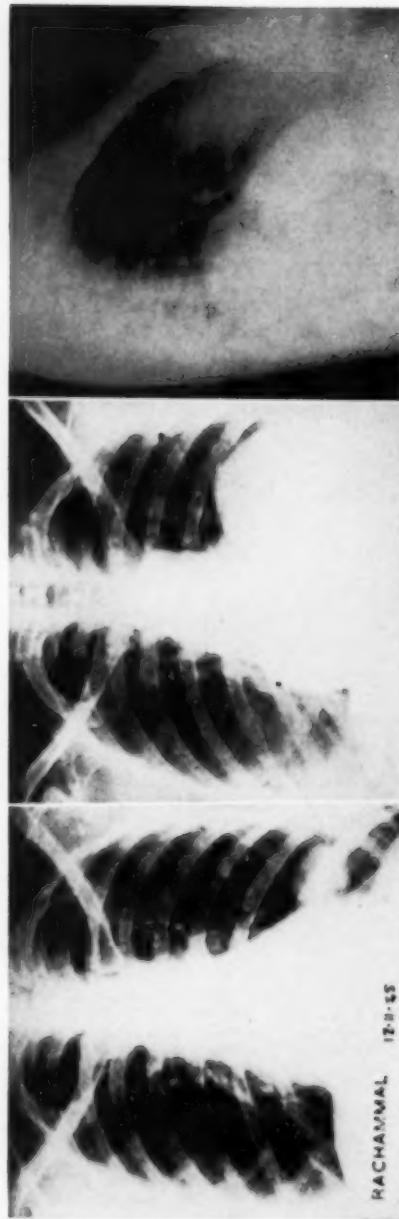


FIGURE 3A

FIGURE 3B

Figure 3 (A)—Case 3. Posteroanterior x-ray film of the chest in 1945 when a diagnosis of carcinoma of the thyroid was made and subtotal thyroidectomy carried out. (B)—X-ray film of the chest five years later showing a large mass in the left lower lobe. (C)—Left lateral x-ray film demonstrating the mass to fill the lower part of the left chest.

FIGURE 3C

on the third postoperative day and remained there until he was discharged on the 12th postoperative day. He was symptom free at the time of discharge but we have been unable to follow him since that time. On examination of the removed specimen it was found to be a typical hydatid cyst but without evidence of living parasites.

Case 3: C.M.C.H. 99818, Mrs. R., a 40 year old married woman entered the hospital on February 28, 1950, with chief complaint of pain in the left chest and cough with expectoration of five months' duration. She complained of feeling feverish in the evenings during the past six months. There was slight anorexia and insomnia. She was referred by Dr. Vadamatayam of Madura who supplied the additional information that he had first seen her in December 1945 when she consulted him regarding an enlarged thyroid. An x-ray film was taken at that time which is reproduced in Fig. 3 A. This revealed a circumscribed shadow in the left lower lung field. Thyroidectomy was carried out by Dr. Vadamatayam and the pathological report was carcinoma of the thyroid. (An attempt has been made to secure the original slides but they are no longer available). The lesion in the left lung field was therefore regarded as a metastasis from the thyroid and she was advised to take deep x-ray therapy. After two or three treatments she absconded and was not seen again until 1950 when she returned complaining of the above noted symptoms. An x-ray film at this time (Fig. 3 B and C) showed the lesion greatly enlarged and practically filling the entire left lower lung field. She was referred to this hospital with a diagnosis of solitary metastasis of the left lower lobe of the lung for consideration of resection.

Physical examination at the time of admission revealed a well nourished woman in no acute distress. The head and neck showed no abnormality except for a well healed thyroidectomy scar. Examination of the thorax showed dullness throughout the lower part of the left chest both posteriorly and anteriorly. No rales were detected. The heart showed no abnormality; the blood pressure was 90/68. The remainder of the physical examination was within normal limits. A preoperative examination of the blood showed hemoglobin 15.5 gms., red blood cell count 4.8 million, white blood cells 8,700 with 64 per cent polymorphonuclears, 23 per cent lymphocytes, 10 per cent eosinophils and 3 per cent monocytes. Urine examination was normal except for a few white cells. Further x-ray studies were carried out which gave a little additional information, showing a large mass within the left lung field. Bronchoscopy demonstrated almost complete occlusion of the left lower lobar bronchus by extrinsic pressure. No intrabronchial abnormality was found.

With a preoperative diagnosis of carcinoma, metastatic, of the left lower lobe thoracotomy was done on March 9, 1950, under procaine local and endotracheal ether anesthesia. She was operated upon in the prone position and the chest was entered thru the sixth left interspace. We were surprised to find the lower lobe completely free within the pleural cavity. A small amount of turbid fluid was present. The entire lower lobe appeared to be replaced by a large cystic-feeling mass. It was found possible to remove the lesion entirely by a lower lobectomy leaving the upper lobe undisturbed. The lower lobe was therefore removed by the usual technic individually ligating the arterial and venous supply and closing the bronchus with a row of interrupted sutures. One abnormal artery to the lower lobe was found arising from the lingular artery of the upper lobe. She was returned to the ward in good condition with a blood pressure of 120/95. Her postoperative course was essentially uneventful. The upper lobe completely expanded to fill the chest and she was about to be discharged on the 11th postoperative day when she had a temperature of 100°. The following day it reached 102.2° and examination of blood at that time revealed malarial parasites. Paludrine was given and the temperature promptly returned to normal and remained there. She was discharged asymptomatic on the 16th postoperative day. An x-ray film taken on March 27, 1950, is shown in Fig. 3 D. Pathological examination of the removed lower lobe showed it to be entirely replaced by a large hydatid cyst (Fig. 3 E and F). Many parasitic elements were found.

Case 4: C.M.C.H. 98931, A.S. This 11 year old boy was first admitted to the hospital on the pediatric service on January 14, 1950, because of chest pain and cough of six weeks' duration. He gave a history of having had a fall from a height of four or five feet at the time of the onset of his symptoms and stated that he fell on the left side of the chest. Symptoms from this gradually subsided, but returned after another mild fall three weeks before admission. At that time his cough increased and he expectorated a small amount of sputum. There had been no hemoptysis.

He found it difficult to lie on the left side. A low-grade fever had been present for one week. Physical examination at that time revealed a well developed boy in no acute distress. His examination was essentially normal except for the chest which showed dullness and absence of breath sounds over the left lower posteriorly. Laboratory studies showed a hemoglobin 9 grams, white blood cells 17,200 with 80 per cent polymorphonuclears, 16 per cent lymphocytes, and 4 per cent monocytes. The



FIGURE 3D

Figure 3 (D)—Case 3. Postoperative x-ray film of the chest following left lower lobectomy. (E)—Photograph of the left lower lobe showing the hydatid appearing near the surface of the lung. (F)—Photograph of the left lower lobe after division.

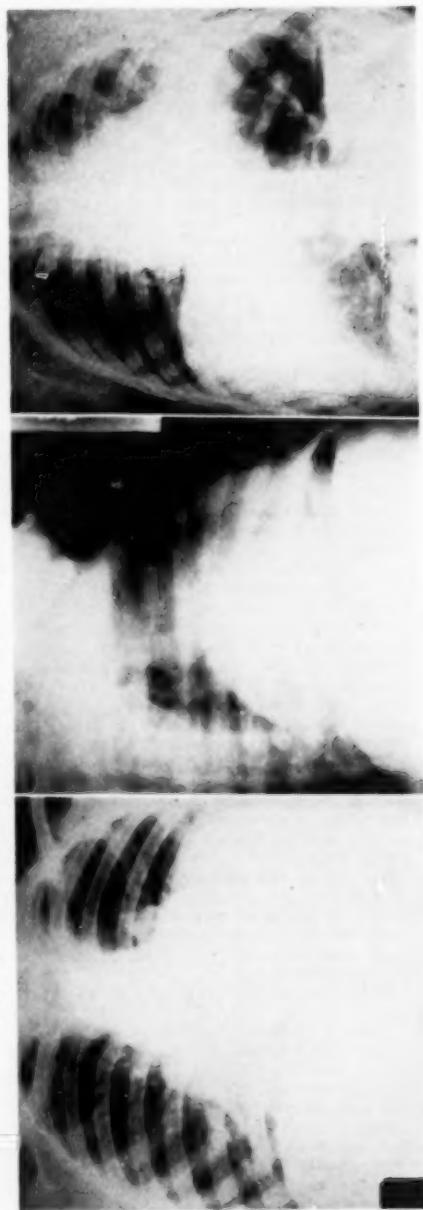


FIGURE 3E

FIGURE 4C

FIGURE 4B

FIGURE 4A

sedimentation rate was 63 mm. in one hour and 95 mm. in two hours. The urine was normal. Examination of the stools revealed hookworm ova. A Mantoux test 1:10,000 was negative. No acid fast bacilli were recovered from the sputum or stomach contents. The Kahn test was negative. His temperature after admission was 101° to 102° daily, but gradually subsided to normal by the end of the first week. The left chest was aspirated on the sixth hospital day and 16 cc. of clear fluid were removed. The fluid was negative on smear and culture. X-ray films of the chest revealed an ill defined mass in the left lower lung field best visualized in the oblique view, Fig. 4 A and B. A diagnosis of diaphragmatic hernia was considered, but further studies revealed no such abnormality. Inasmuch as he became symptom free it was thought advisable to observe him for a time in the outpatient department before resorting to surgical treatment. He was therefore discharged on February 8, 1950, after having been treated for the hookworm infestation.

He returned to the hospital on March 13, 1950, because of increased cough along with some fever and the appearance of a small amount of blood in the sputum of three or four days' duration. Physical examination was essentially unchanged from the first admission. Repeated x-ray films showed no difference when compared with the previous films. Thoracotomy was advised and a preoperative diagnosis of cystic mass in the left lower lobe was made. Left lower lobectomy was done under endotracheal ether anesthesia on March 20, 1950. He was operated upon in the lateral position and the pleural cavity was entered thru the sixth intercostal space. A large mass was found in the left lower lobe which was adherent to the chest wall although the adhesions freed without much difficulty. The entire lower lobe seemed to be involved in the process and in the hilar area a large number of vascular lymph nodes were found. This was true not only of the lobar hilum but the pulmonary hilum as well. A lymph node removed for frozen section biopsy was reported as inflammatory. By careful dissection the lower lobar hilum was finally developed and the lobe and mass removed without opening the cyst. He was returned to the ward in good condition with a blood pressure of 90/70 but with a pulse of 160. Five hundred cc. of blood were given during the operation. He did well after the operation although he had a temperature of 104° on the day of operation. We believe this was a pyrogenic reaction from the intravenous saline he had been given. The temperature settled down and remained normal after the fifth postoperative day. He was discharged asymptomatic on the 14th postoperative day and immediately returned to school. His post-operative x-ray film is shown in Fig. 4 C. The pathological examination of the spec-

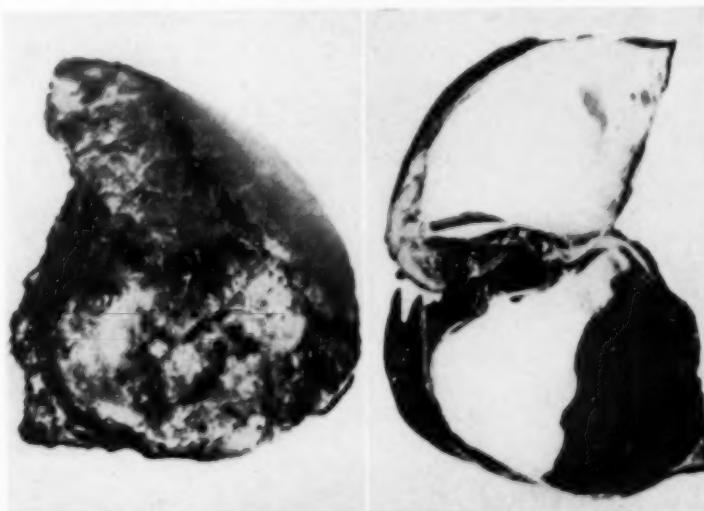


FIGURE
4D

FIGURE
4E

Figure 4 (A)—Case 4. Posteroanterior x-ray film of the chest showing a diffuse haziness over the lower two thirds of the left lung field. (B)—Oblique x-ray film of the chest which more clearly demarcates the extent of the mass in the left lower lobe. (C)—Postoperative x-ray film following left lower lobectomy for hydatid. (D)—Photograph of the left lower lobe containing large hydatid cyst. (E)—Photograph of the left lower lobe after section.



FIGURE 5A

FIGURE 5B

FIGURE 5C

Figure 5 (A)—Case 5. Preoperative x-ray film of the chest showing a lobulated mass in the lower part of the right lung field and also haziness near the apex of the right upper lobe. (B)—Right lateral x-ray film showing the mass in the lower chest to lie mainly anterior. (C)—X-ray film of the chest following segmental resection of the apical segment of the right upper lobe and evacuation of the pleural hydatids which communicated with the hydatids in the liver thru the diaphragm.

imen revealed it to be a cyst 8 cm. in diameter with a laminated membrane containing many scolices. The lung tissue of the lower lobe was markedly compressed. Photographs of the specimen are reproduced in Fig. 4 D and E.

Case 5: C.M.C.H. 107098, Mr. P.B. This 17 year old man was admitted to the hospital on January 9, 1951, with a chief complaint of pain in the right chest of three years' duration. He stated that the difficulty started with an attack of dysentery three years previously. The intestinal symptoms abated after three weeks, but the pain in the right lower part of the chest continued. The pain was rather severe in nature and almost constant. There was some radiation both to the back and to the opposite side. Although he had taken various types of treatment it was not until three months previously that he had been admitted into a hospital for investigation.

There had been breathlessness on slight exertion and he was conscious of palpitation. The cough and sputum had been minimal and he had noticed no blood in the sputum at any time.

During the past four years he had had frequent attacks of pain in the abdomen and various tests had been carried out without demonstrating any marked abnormality. A month before admission a lymph node was removed from the left side. The result of the examination is not known.

Physical examination revealed a well developed and nourished young man complaining of severe pain in the right chest. Examination of the head and neck revealed impaired hearing in the left ear. In the neck a movable nodule about 1 cm. in diameter was found in the region of the isthmus of the thyroid and a similar nodule just to the right of the midline. The thyroid appeared to be slightly enlarged to palpation. The nodules moved with the thyroid. On examination of the chest there was slight dullness toward the right base and over the apex, but no rales were heard. Both sides of the chest seemed to move equally. The heart was normal to examination and the blood pressure was 140/80. The liver and spleen were not palpable and there was no abnormality made out on examination of the abdomen.

Laboratory tests of the blood showed 11.75 grams of hemoglobin, red blood cell count 4.85, white blood cell count 11,400 with 54 per cent polymorphonuclears, 43 per cent small lymphocytes and 3 per cent monocytes. The Kahn test was negative and the sedimentation rate 12 mm. at the end of the first hour and 36 mm. at the end of the second hour. The sputum revealed no acid fast bacilli and no hydatid elements could be demonstrated. The Casoni test was positive. Examination of the urine showed nothing abnormal.

An x-ray film of the chest revealed multiple clear cut oval and round densities at the base of the right lung, and also haziness at the right apex. Fig. 5 A and B. A lateral x-ray film demonstrated that the masses previously described in the lower right chest were located anteriorly and one large calcified round lesion was noted apparently beneath the diaphragm in the liver.

Bronchoscopy showed no intrabronchial abnormality.

On January 23, 1951, right thoracotomy was carried out and the pleura was found to be studded with innumerable small hydatids mostly from 0.5 cm. to 1.0 cm. in diameter. In the lower part of the chest there were many larger hydatids two or three inches in diameter as visualized in the x-ray film, the largest one being 6 cm. in diameter. When the upper lobe was mobilized it was found that there was also a hydatid in the posterior segment of this lobe. This cyst was inadvertently opened in freeing it from the chest wall. Although it was thought at first that the lower hydatids were in the middle lobe it was found that they could be separated from the lobe and it then became apparent that they came up thru the diaphragm. The cysts were all taken out and in doing so a communication with numerous cysts in the liver was found and some of these liver cysts were grossly infected. The previously noted calcified cyst in the liver was easily located. All the subdiaphragmatic and liver cysts were evacuated and this area was drained subcostally, following which the diaphragm was closed. The posterior segment of the upper lobe was then removed in the usual manner. The chest was drained with two drains and closed in the routine fashion. He had a rather stormy convalescence running a spiking type of fever for about three weeks. This was thought to be due to improper drainage of the subphrenic area.

On March 29, 1951, under local anesthesia the two cysts were removed from the thyroid. It was thought that these might be hydatids, but pathological examination revealed them to be adenomas of the thyroid. The drainage tube was removed from the subphrenic area two weeks before discharge and he was allowed to go home on the sixth of April, 1952. Fig. 5 C.

Case 6: Mrs. K., C.M.C.H. 125876. This 48 year old married woman was admitted to the hospital on October 31, 1952 with a history of productive cough and dyspnea of seven months' duration. She stated that these symptoms followed a short febrile incident lasting three or four days and she first consulted the medical outpatient department of this hospital on July 9, 1952. At that time a diagnosis of a hydropneumo-



FIGURE 6A
FIGURE 6B
FIGURE 6C

Figure 6 (A)—Case 6. Preoperative x-ray film of the chest showing a complete pneumothorax on the left side with complete collapse of the left lung. The lung could not be made to re-expand by repeated thoracentesis. (B)—X-ray film of the chest following insertion of a catheter for suction drainage which likewise did not re-expand the lung. (C)—X-ray film of the chest following left pneumonectomy. (D)—Photograph of removed left lung showing hydatid in the left lower lobe which had ruptured into the pleura. The hydatid membranes are extruding thru the visceral pleura. In spite of this there was no fluid in the chest and no signs of any infection.

thorax on the left side was made. She was raising one to two ounces of thin, whitish sputum which was negative for tubercle bacilli. The left chest was aspirated on four occasions removing from 1,500 to 2,000 cc. of air at each instance. These maneuvers, however, gave only temporary relief. She was seen in consultation by the thoracic surgical service on October 17 at which time fluoroscopic examination showed the left lung to be completely collapsed and a small amount of fluid in the left costophrenic angle. Admission was advised, but not effected until October 31, 1952.

Physical examination showed a middle aged woman with considerable dyspnea, cough and a small amount of thick purulent sputum. She was moderately dyspneic even at rest. There was no cyanosis or clubbing of the digits. The trachea was markedly displaced to the right. The left chest moved little with respiration. Fremitus was absent. Percussion revealed hyperresonance on the left side with absent breath sounds. The right lung field was clear.

Laboratory examination revealed hemoglobin 12 grams, red blood cell count of 4.86 million and a total white count of 14,500. Polymorphonuclears were 60 per cent, lymphocytes 29 per cent, eosinophils 9 per cent and monocytes 2 per cent. The blood sedimentation rate was 26 mm. in the first hour and 46 mm. at the end of the second hour. The blood Kahn was negative. Urinalysis and stool examination revealed no abnormality. Repeated examinations of the sputum were negative for acid fast bacilli.

Fluoroscopic and x-ray films revealed complete collapse of the left lung with marked displacement of the mediastinum to the right side. Fig. 6 A. No detail of the left lung could be made out. Aspiration of 2,000 cc. of air failed to change the position of the left lung.

Methylene blue was injected into the left pleural space but was not brought up in the sputum. Inasmuch as repeated aspirations did not change the status of the lung an intercostal catheter was inserted in the left chest on November 2. This was attached to under-water suction, but did not effect much expansion of the lung although the mediastinum did return to the midline. In view of the lack of progress, thoracotomy was advised and carried out on November 11, 1952. Exploration revealed a small amount of fluid in the left chest and a moderately large hydatid cyst of the left lower lobe which had ruptured thru into the pleural space exposing some of the hydatid membrane thru the opening. A left lower lobectomy was carried out and the upper lobe decorticated. However, it was not possible to achieve expansion of the upper lobe even after complete decortication and the pneumonectomy was therefore completed.

She had an uneventful postoperative course. A Casoni test done after operation showed it to be strongly positive. She had an uncomplicated postoperative course and was discharged on November 30, 1952. A photograph of the specimen is shown in Fig. 6 D.



FIGURE 6D

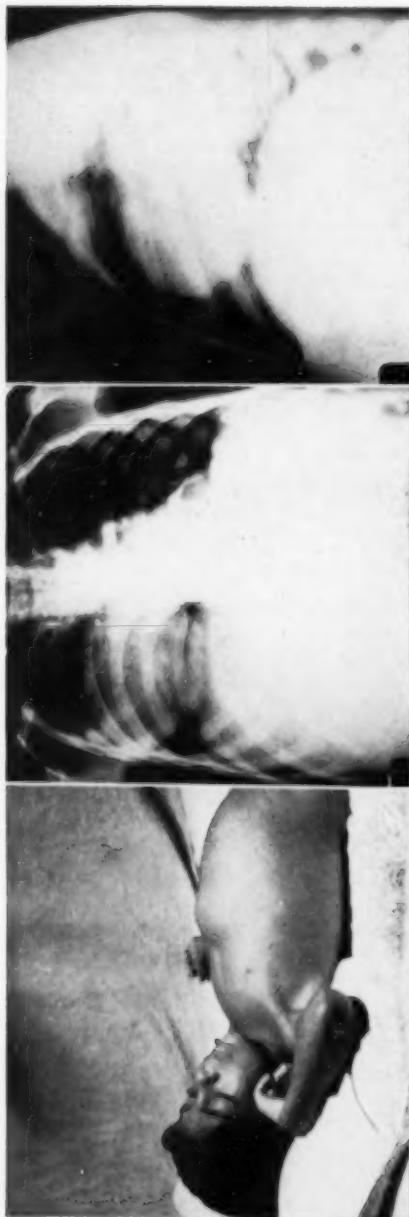


FIGURE 7A

FIGURE 7B

FIGURE 7C

Figure 7 (A)—Case 7. Photograph of patient on admission to the hospital showing a mass just to the right of the epigastrium. (B)—Posteroanterior x-ray film of the chest showing a large mass in the right mid zone. (C)—Right lateral x-ray film of the chest demonstrating the mass to lie anteriorly. (D)—X-ray film of the chest following right middle lobectomy. (E)—Photograph of patient at time of discharge showing the abdominal and the thoracic incisions for removal of the cysts in the liver and lung.

Case 7: C.M.C.H. 124951. This six year old girl was admitted to the hospital on September 29, 1952 because of a mass in the upper abdomen of gradually increasing size of four months' duration and fever for two weeks. Five months before coming to the hospital she complained of vague abdominal pain, anorexia and lethargy. The symptoms continued unabated and four months before admission the parents first noted a mass in the upper abdomen. A diagnosis of cirrhosis of the liver was made and she was treated with methionine, liver extract and vitamins. All her symptoms gradually increased in degree.

Two weeks before admission she struck her upper abdomen against the corner of a table. She developed fever the following day and the mass in the epigastric region began to increase rapidly in size and her fever rose progressively. She also had a slight cough the last week before admission.

The past history of the family was non-contributory except that the family did have several dogs which were allowed in the house.

Physical examination revealed a thin, six year old girl moderately dyspneic and apparently acutely ill. The positive findings were limited to the chest and abdomen. Percussion of the chest showed it to be impaired in the lower right chest anteriorly and in the axilla. Breath sounds were diminished in the same area. Examination of the abdomen revealed a rounded mass four to five centimeters in diameter which was visible as well as palpable in the epigastrium. Fig. 7 A. No thrill could be made out. The liver was apparently much enlarged, the inferior margin being 5 cm. below the costal margin.

Laboratory examination revealed hemoglobin 10 grams, white blood cell count 15,500 with polymorphonuclears 63 per cent, lymphocytes 35 per cent, and eosinophils 2 per cent. Examination of the stool and urine showed nothing abnormal. Three blood cultures were sterile. Liver function tests revealed no deviation from normal. A Casoni test gave a positive delayed reaction locally and she also developed angio-neurotic edema.

X-ray films of the chest revealed a large mass in the lower two thirds of the right lung field which appeared to lie mainly in the region of the middle lobe in the lateral view. Fig. 7 B and C.

After admission she continued to run a swinging type of temperature from 100° to 104.5°. No cause for the fever other than the hydatid disease could be found and there was no response to penicillin or streptomycin. On the seventh hospital day laparotomy was performed by the general surgical service and a cyst in the left lobe of the liver was aspirated. A typical hydatid cyst was found and the membrane was removed by suction. Exploration showed the presence of a second hydatid cyst attached to the lower part of the right lobe of the liver. Removal of this was deferred. Postoperatively, the child did well and 17 days later a second abdominal operation was performed and the hydatid cyst in the right lobe of the liver was removed. Exploration at that time did not reveal any further cysts in the liver.

Because of the persistent enlargement however, a liver biopsy was to be performed on the 44th hospital day. A hypodermic needle was inserted to infiltrate with novocaine.

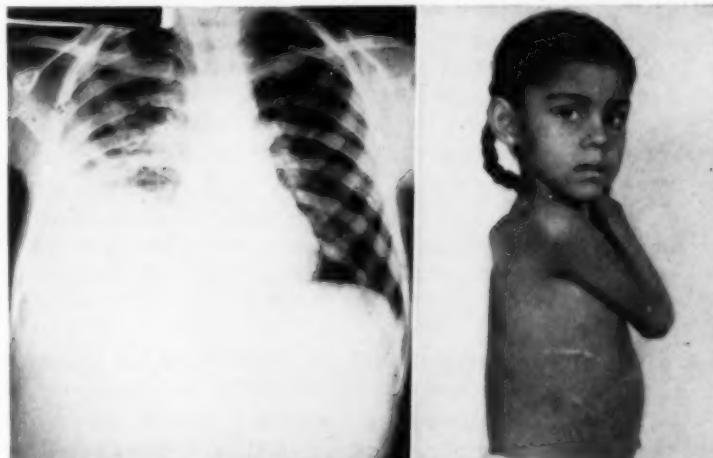


FIGURE 7D

FIGURE 7E

At the depth of 1 cm. from the skin surface 2 cc. of clear colorless fluid were aspirated. This fluid showed a trace of albumin, but no scolices. Within 12 hours after aspiration of this hydatid cyst the patient developed abdominal distension, generalized erythema, rapid respiratory rate and a temperature of 103° F. Benadryl was given and the symptoms gradually subsided within 48 hours. Forty-nine days after admission right thoracotomy was done and the large hydatid cyst in the middle lobe was removed by doing a right middle lobectomy. During this operation it was observed that the right diaphragm was markedly elevated and a mass was apparently present in the upper surface of the liver. The diaphragm was incised and a large hydatid cyst in the upper part of the right lobe of the liver was removed. She had a moderate febrile reaction for four days after operation, but subsequently was afebrile. She was discharged 22 days after operation in good condition. Fig. 7 E.

Discussion

Although the hydatid membrane is a permeable one, as evidenced by the fluid that forms within it, there has been no drug yet found which is innocuous to the host and yet will penetrate the membrane and kill the hydatid. Until such treatment becomes available, surgical treatment is advisable. The mortality in practically all series of cases is low, especially in the uncomplicated group, and therefore these lesions should be treated in the early stage before complications develop.

Our experience with attempted intact evacuation of the cyst has been small and not very successful, but the reports of Barrett and Thomas⁷ as well as Bendandi⁸ indicate that it is possible in many cases. This method of treatment does not eliminate the problem of the persistent empty sac, but with careful attention to obliterate the small bronchial fistulae that are apparent and by the use of sutures to oppose the pericyst surfaces, suppuration is not apt to follow, especially with antibiotic protection. If the cyst is small and can be removed by segmental lobectomy, this has been safer in our hands as far as avoiding rupture of the cyst is concerned. Every effort should be made to preserve pulmonary function, but if the hydatid is a large one and limited to only one lobe, we believe lobectomy is preferable to simple evacuation with a large empty sac remaining and a markedly atelectatic lobar remnant.

The hydatid that communicates with liver and lung transdiaphragmatically may tax the ingenuity of the surgeon and often are long difficult operative problems. The pulmonary part can usually be handled without too great difficulty, but the time necessary to obliterate the large multilocular hydatid hepatic abscess may be prolonged.

SUMMARY

A series of 20 pulmonary hydatids treated during the past three years without mortality are presented. Small uncomplicated cysts can be removed by evacuation or extrusion of the cyst or by limited pulmonary resection.

Those with both pulmonary and hepatic involvement but without transdiaphragmatic communications can be handled as for either one alone.

In three of our cases there were transdiaphragmatic communications between the liver and the lung and the pleura as well in two. Prolonged hospital treatment was necessary in each instance.

RESUME

Les auteurs présentent vingt cas de kystes hydatiques pulmonaires qui ont été traités ces trois dernières années sans aucune mortalité. Certains kystes, petits et non compliqués peuvent être extirpés par la simple exérèse du kyste ou par une résection pulmonaire limitée.

En présence de ceux qui ont comporté à la fois une atteinte pulmonaire et une atteinte hépatique, sans qu'il y ait de communication transdiaphragmatique, on peut agir comme s'il s'agissait de l'une des deux localisations isolées.

Dans trois de leurs cas, il existait des communications transdiaphragmatiques, le foie, le poumon et la plèvre étaient intéressés. Il fut alors chaque fois nécessaire de traiter longuement les malades à l'hôpital.

RESUMEN

Una serie de 20 quistes hidatídicos tratados durante los pasadostres años sin mortalidad. Pequeños quistes no complicados pueden ser extraídos por evacuación, o extrusión del quiste o por limitada resección pulmonar.

Aquellos que tienen compromiso pulmonar o hepático pero sin comunicaciones transdiafragmáticas pueden ser tratados aisladamente cada uno.

En tres de nuestros casos había comunicación transdiafragmática, y en dos el hígado, el pulmón y la pleura se encontraban afectados.

Se necesitó en todos los casos una estancia prolongada en el hospital.

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Thoracoplasty and Contralateral Pneumothorax in the Treatment of Bilateral Pulmonary Tuberculosis*

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Thoracoplasty and Contralateral Pneumothorax in the Treatment of Bilateral Pulmonary Tuberculosis

Despite the widespread use of the tuberculostatic drugs, pneumoperitoneum, and excisional surgery, there are patients with bilateral parenchymal disease who need bilateral collapse therapy for control of their disease. The present study has been undertaken to determine the results of thoracoplasty with the presence of contralateral pneumothorax.

Material

This study consists of 34 consecutive patients with proved tuberculosis treated by thoracoplasty with the presence of contralateral pneumothorax. Among them were 26 whites, five Negroes, two Mexicans, and one Indian, and they were rather evenly divided among men and women. The youngest was 16, and the oldest was 53, with 26 being between 20 and 40 years of age. They were known to have had tuberculosis from one to 15 years prior to the completion of the thoracoplasty with an average duration of five years.

According to the National Tuberculosis Association classification, 32 had far advanced and two had moderately advanced pulmonary tuberculosis. The cases were further evaluated on the basis of the individual lungs prior to collapse therapy.

TABLE I
CLASSIFICATION OF DISEASE IN EACH LUNG PRIOR
TO ONSET OF THERAPY

Classification	Thoracoplasty	Pneumothorax
Minimal	0	1
Moderately advanced	12	30
With cavity	9	18
Without cavity	3	12
Far advanced with cavity	22	2
Total	34	33*

*One had pneumothorax on admission and the original extent of disease is unknown.

*From the American Legion Hospital, Battle Creek, Michigan.

As is seen in Table I, 31 had cavernous disease in the lung treated by thoracoplasty, and 20 had a cavity on the side of pneumothorax.

The duration of the pneumothorax had been from five months to five years prior to thoracoplasty as seen in Table II. Pneumothorax had been

TABLE II
DURATION OF PNEUMOTHORAX PRIOR TO CONTRALATERAL
THORACOPLASTY

Duration in Months	Number
5-12	14
12-24	9
24-36	6
36-48	2
48-60	3
Total	34

improved and made adequate by closed intrapleural pneumonolysis in 16 cases. In each instance there had been closure of the cavity, and serial roentgenograms revealed stability of the lesions on the pneumothorax side before thoracoplasty was started. Prior to thoracoplasty, eight patients had pleural effusions requiring aspirations, and three had spontaneous collapse of the lung, but in no instance did the complications become severe enough to necessitate abandonment of the pneumothorax.

Thoracoplasty

There were 106 stages of thoracoplasty performed in these 34 patients as seen in Table III. All were routinely bronchoscoped before surgery, and

TABLE III
NUMBER OF STAGES OF THORACOPLASTY IN 34 PATIENTS

Operation	Number
Posterior	89
Anterior	15
Revision	2
Total	106

the bronchial lumen was judged adequate for ventilation and the raising of secretions. Four required therapy for ulcerative tuberculous bronchitis prior to thoracoplasty.

The finished thoracoplasty was not always as extensive as originally judged to be necessary, and was limited because of border-line dyspnea based on clinical evaluation. Fortunately, no complications directly related to pneumothorax occurred.

However, in seven the planned program had to be discontinued because of severe complications: In three patients the cardiorespiratory functional reserve was inadequate for continuing the program; atelectasis with increase in disease on the operative side occurred in two cases; ipsilateral spread of tuberculous disease in one; and severe hemoptysis, with death in 24 hours, in another. In one of the above patients there was also a

tuberculous wound infection. Our only postoperative instance of cardiac decompensation occurred in a 16-year-old Indian male shortly after completion of surgery; he responded to therapy.

Five early deaths occurred in the group having severe complications —this might be expected since they were all poor-risk patients, and perhaps individual lung studies might have excluded some of them from this combined program.

Present Status

The present status of these patients has recently been evaluated. As noted in Table IV, follow-up data have been available on all the patients.

TABLE IV
LENGTH OF FOLLOW-UP

Duration in Years	Number
9 months to one year	1
1- 2 years	4
2- 3 years	4
3- 4 years	4
4- 5 years	3
5-10 years	6
10-15 years	5
Dead	7
Total	34

In addition to the five early deaths, there have been two late deaths occurring three years after surgery—one expired as a result of cor pulmonale and cardiac decompensation, and the other patient developed reactivation of his disease and died of progressive tuberculosis.

Of the 27 living patients, 15 have been discharged from the hospital with conversion of sputum and control of their disease. Twelve are still hospitalized, although five are clinically well and will soon be discharged (Table V). There are 19 with negative sputum by smear and culture of

TABLE V
PRESENT STATUS OF 27 LIVING PATIENTS

Hospitalized	12
Discharged	15
Negative sputum	19
Rare positive culture of sputum concentrate	1
Positive sputum	7

five-day pooled concentrated sputum samples. There is one with an occasional positive sputum culture who is in good clinical condition, and has been followed nine years since surgery. The seven cases having positive sputum are interesting: Three have a residual cavity under thoracoplasty and their prognosis is poor. One, whose surgery was recently completed, is in good clinical condition and is expected to convert his sputum. One has reactivation of disease after 12 years of normal activity

—his prognosis is now poor. Another, four years after surgery, who had been discharged from the sanatorium and was working, had a reactivation of disease in the lung treated by pneumothorax after it had been abandoned. The seventh patient in this group had reactivation of his disease in the lung treated by pneumothorax after five years of negative sputum; bilateral thoracoplasty has recently been done.

Among those whose sputum was immediately converted following institution of the bilateral procedures, three have had subsequent reactivation. One, whose disease was not controlled by thoracoplasty, has since been controlled and converted by upper lobe resection under the thoracoplasty. One relapsed three years following surgery and is now negative, having converted with bedrest and streptomycin-PAS. One reactivated two years following surgery and died of disseminated tuberculosis.

The status of pneumothorax at the present time is shown in Table VI.

TABLE VI
DURATION OF PNEUMOTHORAX

Present Status	Duration	Number
Discontinued	*	21
	7-12 months	3
	1- 2 years	1
	2- 3 years	5
	3- 4 years	3
	4- 5 years	4
	5- 6 years	2
	6- 9 years	3
Being maintained at present		8
	1- 2 years	1
	2- 3 years	2
	3- 4 years	2
	4- 5 years	2
	7 years	1
Expired before pneumo- thorax discontinued		5
Total		34

Eight pneumothoraces are still being maintained and 21 have been discontinued. In 10 the pneumothorax was terminated prematurely because of complications: There were four instances of obliterative pleuritis, three of dyspnea, two of cardiac decompensation, and one of persistent pleural effusion. Apparently, as a direct result of the premature termination of pneumothorax, three developed reactivation of their tuberculosis.

The 27 living patients have been questioned concerning dyspnea. Eleven of them stated that they have no subjective symptoms of dyspnea. Four have slight dyspnea on climbing stairs; seven complain of moderate dyspnea; and five have severe dyspnea on exertion—two of these five, however, have severe dyspnea which occurs only during an acute attack of asthma. The chief causes of dyspnea, as stated by the patients, are climbing stairs, or walking fast—especially against the wind.

Of the 15 discharged patients, all are able to work.

Comment

Antibiotics and excisional surgery have opened a new era in the treatment of pulmonary tuberculosis. They have reduced and changed the indications for collapse therapy but they have not eliminated its usage. The successful treatment of many patients with far advanced bilateral disease still remains with collapse therapy. The salvage obtained from the treatment of such cases will probably always remain small; but the good results obtained would not have occurred unless heroic measures had been adopted.

There have been previous reports presenting the management of such cases by the use of thoracoplasty and contralateral pneumothorax; however, only a few concerned more than isolated cases, and many included cases treated by pneumothorax following surgery. O'Brien, Tuttle, Day, and O'Connor,¹ in 1938 reported 85 cases treated by thoracoplasty in the presence of contralateral pneumothorax. In this group, 207 thoracoplasty stages were done with an overall mortality rate of 21.1 per cent. Sputum was converted in 68.4 per cent of the living cases, and cavities were closed in 58 of the 76 (76.3 per cent) living patients. Difffenbach and Crecca,² in 1941, reported 41 instances among 100 consecutive thoracoplasty cases; among these 41 patients, five died and 13 continued with positive sputum. Buxton and O'Rourke³, in 1944, reported 44 cases on whom 174 stages of thoracoplasty were done in the presence of contralateral pneumothorax. In 13 the planned thoracoplasty program was not completed because of complications. The early mortality rate (within three months) was 6.8 per cent, and the total mortality rate was 29.5 per cent. Among the 31 living patients there had been conversion of sputum in 64.5 per cent.

SUMMARY

1. In the group of 34 patients we are reporting, there were five early and two late deaths, with an overall mortality rate of 20.5 per cent. This does not seem excessive for desperate risk patients.
2. Of the 27 living, 15 have been discharged from the hospital with satisfactory results.
3. Twelve are resident in the sanatorium. Five are nearly ready for discharge; the program for one has been completed too recently for final evaluation but it appears that a favorable outcome will be obtained. In another, additional surgery is planned.
4. In five patients the result can be classified as failure, although this includes the patient with reactivation of disease after twelve years of normal activity.

RESUMEN

En el grupo de 34 enfermos que estamos refiriendo, hubo cinco muertes inmediatas y dos tardías, con una mortalidad conjunta de 20.5 por ciento. Esta mortalidad no parece excesiva para enfermos que constituyen riesgos desesperados.

2. De los 27 que viven, 15 han sido dados de alta del hospital con resultados satisfactorios.

3. Doce, residen en el sanatorio. Cinco, están listos para el alta; el plan ha sido terminado para otro enfermo muy recientemente para estimarse el resultado, pero parece que éste será satisfactorio. En otro, se piensa que se necesitará cirugía adicional.

4. En cinco enfermos el resultado puede clasificarse como fracaso, aunque esto incluye el enfermo con reactivación de la enfermedad después de doce años de vida normalmente activa.

RESUME

1. Sur les 34 malades dont les auteurs rapportent l'observation, il y eut cinq décès précoces, et deux décès tardifs, l'ensemble de la mortalité représentant 20,5%. Ces chiffres ne semblent pas excessifs puisqu'il s'agit de cas qui se présentaient comme désespérés.

2. Sur les 27 malades vivants, 15 ont quitté l'hôpital avec des résultats satisfaisants.

3. Douze d'entre eux séjournent en sanatorium. Cinq sont près de quitter l'établissement. Pour l'un d'entre eux, le recul nécessaire pour une estimation valable des résultats n'est pas encore suffisant. Il semble toutefois qu'on obtiendra un résultat favorable. Dans un cas, on envisage un temps opératoire supplémentaire.

4. Chez cinq malades, on peut considérer qu'il s'agit d'échecs. Il faut noter que parmi eux est compris un malade chez qui l'affection récidiva après 12 années d'activité normale.

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Remarks on the International Nomenclature of Bronchopulmonary Segments

DEZSO KASSAY, M.D.*

Budapest, Hungary

Establishment of the International Nomenclature on Bronchopulmonary Segments by a committee of the International Congress of Oto-Rhino-Laryngology, London, 1949, was welcomed as an important progress. The writer, not being present at the meeting in London, was not in a position to give his opinion. He learned of the agreement from the paper of Huizinga, *Practica Oto-Laryngologica* 12:109, 1950. He sent his remarks, in German, to *Practica*, where they were not accepted. They were consequently published in: *Magyar Sebészet* (Hungarian Surgery), 1950, in Hungarian, and in German, in the *Monatsschrift fuer Ohrenheilkunde und Laryngo-Rhinologie*, 65:55, 1951. The international nomenclature was criticized by Boyden (*Diseases of the Chest*, 23:266, 1953). From this paper the writer learned that the problem is still a timely one and not definitely settled.

In his two papers, mentioned above, the writer stated that the nomenclature of Jackson-Huber seemed to him more correct than the nomenclature of the Committee, because Jackson and Huber did not make concessions in anatomical principle and included only segmental bronchi in their nomenclature. The international nomenclature included two sub-segmental bronchi—the left first and second—disregarding other sub-segmental bronchi at least as important as these two branches. Such are: the axillary (lateral) bronchi of the upper lobes, the subsuperior (sub-apical, second dorsal) branches of the lower lobes and the medial basal bronchus of the left lower lobe. The writer's opinion was that these segmental bronchi should not have a place in a nomenclature. On a basis of similar arguments, Boyden discussed the same points as the writer, asking whether it "may not be advisable to hold to the Jackson-Huber terminology until such a time as an official international committee can deal with these problems." The writer agrees with this proposal, as a greater number should be given opportunity to express an opinion on the subject.

The writer, in his above mentioned paper, stated that until now classification was carried out on the basis of three principles:

1. The term should correspond to the lobe as an anatomical unit.
2. The term should correspond to the lung as an anatomical unit.
3. The bronchopulmonary segments should be named according to the contact organs.

The international nomenclature uses all of these three ways, although simultaneous application of two of them is disputable. In the opinion

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of the writer, the term is correct if it corresponds to the lung as an anatomical unit. Boyden, in another connection, emphasized the necessity of "the lung to be considered as a whole."

Application of the term "apical" to the superior segments of the lower lobes was already criticized by the writer in his paper "The Bronchial Tree: A Classification and Nomenclature, Acta Oto-Laryngologica 37:355, 1949," in the following way: "*The term 'Apical' is not correct when used regarding the lower lobe. It should be reserved for the very apex of the entire lung. On the other hand, it is not correct to speak about 'basal segments' when discussing the upper lobes.*" It is gratifying that Boyden is of the same opinion.

The correspondence of the opinions of Boyden with those of the writer should be clear from the foregoing. Boyden had no knowledge of the papers of the writer, and so it seems remarkable that, independently, the anatomist and the practitioner should have the same objections regarding the "international" nomenclature for the bronchopulmonary segments. By this fact, the suggestion of Boyden, that the international nomenclature should be further discussed and corrected, is supported.



Staff and directors of Hospital de Enfermedades del Tórax, Santiago, Chile, pictured at entrance of new building during inauguration ceremonies.

College News Notes

Inauguration ceremonies for the new Hospital de Enfermedades del Torax in Santiago, Chile were held August 23-26. Dr. Hector Orrego Puelma, Regent of the College for Chile, is Director of this new 460-bed hospital. Speakers at the inauguration included the following members of the College: Drs. Gumerindo Sayago, Buenos Aires, Argentina; Olivier Monod, Paris, France; DeWitt C. Daughtry, Miami, Florida; Fernando D. Gomez, Montevideo, Uruguay; and Pietro Valdoni, Rome, Italy.

At the close of this meeting, Dr. Daughtry also spoke before members of the College in Lima, Peru and Panama City, Panama.

Dr. W. M. Brumby, Houston, Texas, founder of the Texas Tuberculosis Association, was recently honored by the board of directors of the association. Dr. Brumby was awarded a bronze medallion commemorating the 50th Anniversary of the voluntary tuberculosis control movement and a citation "in recognition of the great vision which spanned a dark era of human devastation to focus on an enlightened horizon, and in gratitude for the great humanitarian conscience that rejected every obstacle in galvanizing human effort to ease human despair . . ."

Dr. Harry E. Tebrock, New York, New York, Medical Director of Sylvania Electric Products, Inc., has been appointed Assistant Clinical Professor of Industrial Medicine at New York University-Bellevue Medical Center's Institute of Industrial Medicine.

The Second Peruvian National Congress on Tuberculosis was recently presented in Lima. **Dr. Mario Pastor B.** and **Dr. Max Espinoza G.**, members of the College, served as president and secretary respectively.

The Ministry of Public Health of Asuncion, Paraguay, held their 5th Post-graduate Course on Tuberculosis and Thoracic Pathology under the direction of Dr. Juan M. Boettner, Governor of the College for Paraguay.

College Chapter News

NEW ENGLAND CHAPTER

The New England Chapter has resumed its monthly meetings, held at the Deaconess Hospital in Boston. The next meeting will be held November 17, at which Dr. Harriet Hardy will speak on "Diagnosis of Occupational Diseases of the Lungs." At the December 9 meeting, Dr. William Likoff will speak on "Results in Acquired Heart Disease."

KENTUCKY CHAPTER

At the annual meeting of the Kentucky Chapter, held in Louisville, September 21, the following were elected to office:

President Lawrence A. Taucher, Louisville
Vice-President J. Ray Bryant, Louisville
Secretary-Treasurer Alvin B. Mullen, Waverly Hills (re-elected)

ROCKY MOUNTAIN CHAPTER

The Rocky Mountain Chapter of the College held its annual meeting in Colorado Springs, Colorado, September 25. The following officers were elected:

President Arnold Minnig, Denver
Vice-President William F. Stone, Colorado Springs
Secretary-Treasurer Leroy Elrick, Denver

MIDDLE EAST CHAPTER

(left to right) Drs: Wagih K. Sabbagh, Beirut Mery, Lebanon; Papken S. Mugrditchian, Beirut, Lebanon (President); Michel Khoury, Beirut, Lebanon; Elias Khoury, Beirut, Lebanon; Toufic El-Awar, Bhamdoun, Lebanon; Cesar Chehab, Beirut, Lebanon; and Garbis Karagueuzian, Damacus, Syria.

The 62nd chapter of the College, the Middle East Chapter, comprising members in Lebanon, Syria, Iraq, and Jordan, was organized at a meeting held on September 12 at the Ambassador Hotel, Bhamdoun, Lebanon, under the direction of Dr. Papken S. Mugrditchian, Governor of the College for Lebanon. The following officers were elected:

President	Papken S. Mugrditchian, Beirut, Lebanon
Vice-President	Najib Mahmoud Baghdad, Iraq
Secretary-Treasurer	Cesar Chehab Beirut, Lebanon

ANNOUNCEMENTS

The National Association for the Prevention of Tuberculosis (London, England) will hold their Fourth Commonwealth Health and Tuberculosis Conference in London June 21-25, 1955.

The Jarrell-Ash Company of Newtonville, Massachusetts, has announced a new instrument in production for making complete blood counts automatically in less than two minutes. Called an Arithmometer, it is completely automatic in operation and eliminates the uncertain human factors encountered when blood counts are made by visual microscopic observation.

The Ex-Patient's Sanatorium for Tuberculosis and Chronic Disease has recently been reorganized and is now accepting applications for the admission of patients with chronic chest diseases. The sanatorium is a free non-sectarian institution located in Denver, Colorado.

As a service to professional groups and educational institutions, Lakeside Laboratories, Inc., of Milwaukee, Wisconsin, has made available two new films showing in operative close-ups the dramatic possibilities of lung collapse therapy with an unusual plastic sponge, even in advanced bilateral tuberculosis.

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CALENDAR OF EVENTS

NATIONAL MEETINGS

Interim Session, American College of Chest Physicians
Delano Hotel, Miami Beach, Florida, November 28-29, 1954
21st Annual Meeting, American College of Chest Physicians
Ambassador Hotel, Atlantic City, New Jersey, June 2-5, 1955

POSTGRADUATE COURSE

8th Annual Postgraduate Course on Diseases of the Chest
Bellevue-Stratford Hotel, Philadelphia, March 7-11, 1955

CHAPTER MEETINGS

Cuban Chapter, Havana, December 1, 1954



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